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## IBD-RELATED POLYMORPHISMS

### RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application Serial No. 60/170,257, filed December 10, 1999, and U.S. Provisional Application Serial No.

- 5 60/196,046, filed April 10, 2000, the entire teachings of both of which are incorporated herein by reference in their entirety.

### BACKGROUND OF THE INVENTION

- The genomes of all organisms undergo spontaneous mutation in the course of their continuing evolution, generating variant forms of progenitor nucleic acid
- 10 sequences (Gusella, *Ann. Rev. Biochem.* 55, 831-854 (1986)). The variant form may confer an evolutionary advantage or disadvantage relative to a progenitor form, or may be neutral. In some instances, a variant form confers a lethal disadvantage and is not transmitted to subsequent generations of the organism. In other instances, a variant form confers an evolutionary advantage to the species and is eventually incorporated
- 15 into the DNA of many or most members of the species and effectively becomes the

progenitor form. In many instances, both progenitor and variant form(s) survive and co-exist in a species population. The coexistence of multiple forms of a sequence gives rise to polymorphisms.

Several different types of polymorphism have been reported. A restriction  
 5 fragment length polymorphism (RFLP) is a variation in DNA sequence that alters the length of a restriction fragment (Botstein *et al.*, *Am. J. Hum. Genet.* 32, 314-331 (1980)). The restriction fragment length polymorphism may create or delete a restriction site, thus changing the length of the restriction fragment. RFLPs have been widely used in human and animal genetic analyses (see WO 90/13668; W090/11369;  
 10 Donis-Keller, *Cell* 51, 319-337 (1987); Lander *et al.*, *Genetics* 121, 85-99 (1989)). When a heritable trait can be linked to a particular RFLP, the presence of the RFLP in an individual can be used to predict the likelihood that the animal will also exhibit the trait.

Other polymorphisms take the form of short tandem repeats (STRs) that include  
 15 tandem di-, tri- and tetra-nucleotide repeated motifs. These tandem repeats are also referred to as variable number tandem repeat (VNTR) polymorphisms. VNTRs have been used in identity and paternity analysis (US 5,075,217; Armour *et al.*, *FEBS Lett.* 307, 113-115 (1992); Horn *et al.*, W0 91/14003; Jeffreys, EP 370,719), and in a large number of genetic mapping studies.

20 Other polymorphisms take the form of single nucleotide variations between individuals of the same species. Such polymorphisms are far more frequent than RFLPs, STRs and VNTRs. Some single nucleotide polymorphisms (SNP) occur in protein-coding nucleic acid sequences (coding sequence SNP (cSNP)), in which case, one of the polymorphic forms may give rise to the expression of a defective or otherwise  
 25 variant protein and, potentially, a genetic disease. Examples of genes in which polymorphisms within coding sequences give rise to genetic disease include  $\beta$ -globin (sickle cell anemia), apoE4 (Alzheimer's Disease), Factor V Leiden (thrombosis), and CFTR (cystic fibrosis). cSNPs can alter the codon sequence of the gene and therefore specify an alternative amino acid. Such changes are called "missense" when another



amino acid is substituted, and "nonsense" when the alternative codon specifies a stop signal in protein translation. When the cSNP does not alter the amino acid specified the cSNP is called "silent". Other single nucleotide polymorphisms occur in noncoding regions. Some of these polymorphisms may also result in defective protein expression  
5 (e.g., as a result of defective splicing). Other single nucleotide polymorphisms have no phenotypic effects.

Single nucleotide polymorphisms can be used in the same manner as RFLPs and VNTRs, but offer several advantages. Single nucleotide polymorphisms occur with greater frequency and are spaced more uniformly throughout the genome than other  
10 forms of polymorphism. The greater frequency and uniformity of single nucleotide polymorphisms means that there is a greater probability that such a polymorphism will be found in close proximity to a genetic locus of interest than would be the case for other polymorphisms. The different forms of characterized single nucleotide polymorphisms are often easier to distinguish than other types of polymorphism (e.g.,  
15 by use of assays employing allele-specific hybridization probes or primers).

Only a small percentage of the total repository of polymorphisms in humans and other organisms has been identified. The limited number of polymorphisms identified to date is due to the large amount of work required for their detection by conventional methods. For example, a conventional approach to identifying polymorphisms might be  
20 to sequence the same stretch of DNA in a population of individuals by dideoxy sequencing. In this type of approach, the amount of work increases in proportion to both the length of sequence and the number of individuals in a population and becomes impractical for large stretches of DNA or large numbers of persons.

## SUMMARY OF THE INVENTION

25 Work described herein pertains to the identification of polymorphisms which are associated with inflammatory bowel diseases (IBD), and particularly those within a single risk haplotype, by resequencing large numbers of genes and gene fragments in a large number of individuals. Various genes from a number of individuals have been

resequenced as described herein, and SNPs in these genes have been discovered (see Table 3). Some of these SNPs are cSNPs which specify a different amino acid sequence, some of the SNPs are silent cSNPs and some of these cSNPs specify a stop signal in protein translation. Some of the identified SNPs were located in non-coding regions.

With the goal of identifying IBD susceptibility genes, a genomewide scan was undertaken in 163 pedigrees, and three regions of suggestive linkage (3, 5q31-33, 6p) and one of significant linkage to 19p13 (LOD = 4.6) were identified. Higher density mapping in the suggestive 5q31-33 region revealed a CD susceptibility locus of genome-wide significance (LOD = 3.9). Importantly, the 5q31-p33 localizes to the major immunoregulatory cytokine gene cluster and the 19p13 locus to a region containing numerous genes encoding cytokine/chemokine receptors and other inflammatory-associated molecules that could have a direct role in disease susceptibility.

In order to pursue the evidence of linkage to chromosome 5, a systematic linkage disequilibrium (LD) approach was adopted. The approach that was used in the first stage of LD mapping was to genotype all known microsatellite markers in the 18 cM between D5S1435 and D5S1480, as these two markers delimit a region of a 2 LOD drop on either side of the linkage peak centered at marker D5S2497. All alleles for each marker were examined for evidence of excess transmission from heterozygous parents to CD child using the transmission disequilibrium test (TDT). Only alleles at two of the 57 markers had significant  $C^2$  results ( $p < 0.001$ ): IRF1p1 ( $C^2 = 13.3$ ,  $p = 0.0003$ ) and D5S1984 ( $C^2 = 14.0$ ,  $p = 0.0002$ ) (Table 1). A second stage of mapping was then undertaken to confirm, as well as to better delimit, the region of LD surrounding IRF1p1 and D5S1984. The development of new microsatellite markers was necessary. The marker with the most significant  $C^2$  result was CAh17a ( $C^2 = 16.2$ ,  $p = 0.00006$ ) and was located between IRF1p1 and D5S1984 (Table 2). Furthermore, the alleles 193, 156, 373, 140, 222, and 307 at markers GAh18a, IRF1p, CAh15a, CAh17a, D5S1984,

CSF2p10, respectively, define a haplotype conferring susceptibility to Crohn's disease (CD). In order to identify the sequence variant that would explain the genetic susceptibility to CD provided by this haplotype, a search was performed for all single nucleotide polymorphisms (SNPs) in this region of LD. The SNP discovery was  
 5 accomplished by direct sequencing of overlapping PCR products amplified from DNA samples from eight individuals (six CD patients, one unaffected family member, and one CEPH DNA as control). Table 3 shows the results of the SNP discovery analyses.

139 triads were genotyped for a total of 241 SNPs thus far, where at least 50 trios were fully genotyped. Using a  $C^2$  value of 13 (corresponding to a p-value of 0.05) as  
 10 threshold, 12 SNPs were found to have a significant level of association with CD and extended over a region of 250 kb, from IRF1 to prolyl4 hydroxylase. These were markers IGR2055a\_1, IGR2060a\_1, IGR2063b\_1, IGR2069a\_2, IGR2078a\_1, IGR2096a\_1, IGR2198a\_1, IGR2230a\_1, IGR2277a\_1, IGR3081a\_1, IGR3096a\_1, PROLYLex3\_1 (see Table 4). Any of these best SNPs by themselves are in strong  
 15 association with CD and fully explain the microsatellite LD observations. Furthermore, the best SNPs have nearly identical association characteristics (that is, the allele at one SNP determines the allele of all others on any phased chromosome), confirming that a single risk haplotype extending approximately 250 kb is the source of all the observations of association in this region. Specifically, this haplotype is defined by the  
 20 alleles G, C, G, T, A, A, G, T, G, G, C, T at markers IGR2055a\_1, IGR2060a\_1, IGR2063b\_1, IGR2069a\_2, IGR2078a\_1, IGR2096a\_1, IGR2198a\_1, IGR2230a\_1, IGR2277a\_1, IGR3081a\_1, IGR3096a\_1, PROLYLex3\_1, respectively. The frequency of this haplotype is estimated to be approximately 37% in the general population. Furthermore, this haplotype is transmitted from heterozygous parents to CD patients at a  
 25 ratio of 2.5:1.

The invention relates to a isolated gene or nucleic acid molecule which comprises a single nucleotide polymorphism at a specific location. In a particular embodiment the invention relates to the variant allele of a gene having a single nucleotide polymorphism, which variant allele differs from a reference allele by one nucleotide at

the site(s) identified in Table 3. Complements of these nucleic acid segments are also included. The segments can be DNA or RNA, and can be double- or single-stranded. Segments can be, for example, 5-10, 5-15, 10-20, 5-25, 10-30, 10-50 or 10-100 bases long.

- 5        The invention further provides allele-specific oligonucleotides that hybridize to a gene comprising a single nucleotide polymorphism or to the complement of the gene. These oligonucleotides can be probes or primers.

10        The invention further provides a method of analyzing a nucleic acid from an individual. The method determines which base is present at any one of the polymorphic sites shown in Table 3. Optionally, a set of bases occupying a set of the polymorphic sites shown in Table 3 is determined. This type of analysis can be performed on a number of individuals, who are tested for the presence of a disease phenotype. The presence or absence of disease phenotype is then correlated with a base or set of bases present at the polymorphic site or sites in the individuals tested.

- 15        Thus, the invention further relates to a method of predicting the presence, absence, likelihood of the presence or absence, or severity of a particular phenotype or disorder associated with a particular genotype. The method comprises obtaining a nucleic acid sample from an individual and determining the identity of one or more bases (nucleotides) at polymorphic sites of genes described herein, wherein the presence of a particular base is correlated with a specified phenotype or disorder, thereby predicting the presence, absence, likelihood of the presence or absence, or severity of the phenotype or disorder in the individual. In one embodiment of the invention, the phenotype is inflammatory bowel disease or Crohn's disease.

#### BRIEF DESCRIPTION OF THE DRAWING

- 25        The Figure shows multipoint nonparametric linkage results for the IBD genome scan. Multipoint LOD scores were calculated using the MAPMAKER/SIBS functions implemented in GENHUNTER 2.0. The thick black line indicates the LOD score along the length of each chromosome, and the tick marks indicate the position of the

microsatellite markers. The two horizontal lines depict the genome-wide thresholds for suggestive (LOD = 2.0) and significant linkage.

#### DETAILED DESCRIPTION OF THE INVENTION

Crohn's disease (CD) and ulcerative colitis (UC) are chronic, idiopathic inflammatory disorders of the gastrointestinal tract. These inflammatory bowel diseases (IBD) have a peak incidence in early adulthood, and their combined prevalence is approximately 100-200/100,000. The inflammation in IBD is characterized by altered expression of both pro-inflammatory and immunoregulatory cytokines in the affected intestinal mucosa (Kmiec, *Arch Immunol Ther Expe (Warsz)* 46(3):143-155 (1998)). Genetic factors are believed to play an important role, as the sibling risk ( $\lambda_s$ ) calculated for IBD ranges from 15-40, with a stronger genetic contribution occurring for CD ( $\lambda_s \sim 35$ ) as compared to UC ( $\lambda_s \sim 15$ ). Additionally, relatives of individuals with IBD diagnosed at younger ages appear to be at an even higher risk.

CD is characterized by discontinuous, transmural inflammation affecting any part of the gastrointestinal tract and is manifested by abdominal pain, chronic diarrhea, weight loss, bowel obstructions and fistulae. UC occurs as a continuous, mucosal inflammation affecting only the large intestine with primary symptoms including diarrhea, rectal bleeding and abdominal pain. The search for susceptibility genes for these two diseases has resulted in the identification of two potential susceptibility loci. The first, called *IBD1*, is a CD-susceptibility locus that lies in the pericentromeric region of chromosome 16 (Hugo *et al.*, *Nature* 379:821-822 (1996)). The second (*IBD2*) is located in a 41 cM region surrounding marker D12S83 and appears to be linked to both CD and UC (Satsangi *et al.*, *Genetics* 14:199-202 (1996)). These putative loci, however, have only been replicated in some, but not all, subsequent studies (Cavanaugh *et al.*, *Proc Natl Acad Sci USA* 62:291-298 (1998); Cho *et al.*, *The National Academy of Sciences* 95:7502-7507 (1998); Curren *et al.*, *Gastroenterology* 115:1-7 (1998); Duerr *et al.*, *The American Society of Human Genetics* 63:95-100 (1998); Rioux *et al.*, *Am. J. Hum. Genet.* 63:1086-1094 (1998); Yang *et al.*,

*Gastroenterology* 109:440-448 (1995)), supporting the belief that there exists substantial genetic heterogeneity. Furthermore, *IBD1* and *IBD2* only account for a fraction of the heritability of IBD, suggesting that additional loci contribute to disease susceptibility. Thus, as described herein, the susceptibility loci in a Canadian IBD population was assessed by studying families with multiple affected siblings (McLeod *et al.*, *Dis Colon Rectum* 40:553-557 (1997)).

A genome-wide screen was performed on 181 IBD-affected sibling pairs (ASP) and 5 IBD-affected relative pairs (RP) from 163 families. Among these ASP, 122 were CD pairs, 25 were UC pairs, and 34 were “mixed” pairs (one sibling with either CD or UC, the other with CD, UC or IC). All ASP and available parents (140 families had both parents available, 17 had one parent available, and 1 was missing both parents), as well as all RP, were genotyped with 312 microsatellite markers covering the genome with approximately 12 cM distance between markers. Simulations of this dataset indicated that the genome-wide threshold for suggestive linkage (the score expected to occur one time at random in a genome scan) was at a LOD of 2.0. Using either this calculated threshold, or the published threshold of LOD 2.2 based on an infinitely dense map (Lander & Kruglyak, *Nature Genetics* 11:241-247 (1995)), multipoint nonparametric linkage analysis of these data revealed 4 loci which surpassed this threshold (Figure). Specifically, chromosome 3 had a peak LOD of 2.4 between markers D3S1766 and D#S1285, chromosome 5 a peak LOD of 3.0 between GATA68A03 and D5S816, chromosome 6 a peak LOD of 2.3 between D6S1019 and D6S1017, and chromosome 19 a peak LOD of 4.6 between GATA21G05 and D19S586. In fact this chromosome 19 locus exceeds the threshold for genome-wide significance of 3.6 (Lander & Kruglyak, *Nature Genetics* 11:241-247 (1995)), and represents a novel IBD susceptibility locus.

This novel locus maps to an extended region on 19p13 (Figure) that contains many different genes of immunologic interest such as intercellular adhesion molecule 1 (ICAM1), complement component 3 (C3), the thromboxane A2 receptor (TBXA2), leukotriene B4 hydroxylase (LTB4H), and the janus tyrosine kinases TYK2 and JAK3.

There is some evidence supporting their relevance in IBD susceptibility: 1) modest positive association results have been reported for the ICAM1 (Yang *et al.*, *Gastroenterology* 109:440-448 (1995)) and C3 molecules (Elmgreen *et al.*, *Acta Med Scand* 215(4):375-8 (1984)); 2) attempts to interfere with the TBXA2 (Taniguchi, 1997) and LTB4 (Hawkey *et al.*, *Agents Actions, Special Conference Issue* (1992)) mediated inflammatory pathways have shown some therapeutic value; and 3) the janus kinases have been shown to be important in the transduction of the molecular signal from cytokine receptors.

The finding of suggestive linkage to an approximately 30 cM region spanning the cytokine gene cluster on 5q31-q33, containing many of the immunoregulatory cytokines such as IL4, IL13, IL5 and IL3, led to the performance of higher density mapping in this region. Specifically, the original families and an additional 12 families were genotyped for 34 extra microsatellite markers. Multipoint nonparametric analysis were then performed using three different phenotypic categories: IBD, CD and CD16. In the first, all individuals with CD, UC or IC were designated as affected; in the second, only individuals with CD were designated as affected; in the third, only individuals with CD were designated as affected and only families with at least one affected sibling diagnosed at the age of 16 or younger were included. This last category was examined due to an expected enrichment for genetic factors over environmental causes. These analyses demonstrate the presence of a locus of genome-wide significance in the group with early onset CD (MLS = 3.9). Evidence for linkage to the syntenic region in mice has been reported in an induced model of colitis (Mahler, *Genomics* 55:147-156 (1999)).

Although the suggestive loci on chromosomes 3 and 6 identified as described herein have not yet been followed up with higher density mapping, it is important to note that the linkage peak on chromosome 3 is approximately 10 cM away from a previously reported suggestive locus (Satsangi *et al.*, *Nature Genetics* 14:199-202 (1996)), and the linkage peak on 6 lies approximately 20 cM centromeric to the major histocompatibility complex (MHC) Class II region. A recent study has described

linkage to this chromosome 6 region (Hampe *et al.*, *Am. J. Hum. Genet.* 64 (1999)), and a large meta-analysis of the results derived from 29 different studies has also reported that both CD and UC were associated with specific Class II alleles (Stokkers *et al.*, *Gut* 45:395-401 (1999)). Finally, in order to assess whether the *IBD1* and *IBD2* loci are contributing to the IBD susceptibility in this population, exclusion mapping of the data was performed. These analyses demonstrate that the entire chromosome 12 can be excluded for loci of even modest effects ( $\lambda_s > 1.5$ ), but can only loci conferring a  $\lambda_s > 4$  on chromosome 16 can be excluded, suggesting that *IBD1* ( $\lambda_s \sim 1.3$ ) could have gone undetected in the present study.

Thus, this work has identified two novel susceptibility loci: a locus on chromosome 5q31-33 that confers susceptibility to CD and a locus on chromosome 19p13 that confers susceptibility to IBD. Furthermore, particular SNPs within these loci have been identified which may be associated with disease susceptibility.

The present invention relates to a gene which comprises a single nucleotide polymorphism (SNP) at a specific location. The gene which includes the SNP has at least two alleles, referred to herein as the reference allele and the variant allele. The reference allele (prototypical or wild type allele) has been designated arbitrarily and typically corresponds to the nucleotide sequence of the gene which has been deposited with GenBank or TIGR under a given Accession number. The variant allele differs from the reference allele by one nucleotide at the site(s) identified in Table 3. The present invention also relates to variant alleles of the described genes and to complements of the variant alleles. The invention further relates to portions of the variant alleles and portions of complements of the variant alleles which comprise (encompass) the site of the SNP and are at least 5 nucleotides in length. Portions can be, for example, 5-10, 5-15, 10-20, 5-25, 10-30, 10-50 or 10-100 bases long. For example, a portion of a variant allele which is 21 nucleotides in length includes the single nucleotide polymorphism (the nucleotide which differs from the reference allele at that site) and twenty additional nucleotides which flank the site in the variant allele. These nucleotides can be on one or both sides of the polymorphism.



Polymorphisms which are the subject of this invention are defined in Table 3. The reference sequence for many of the genes or gene fragments is provided in Table 5. For sequences which are not present in Table 5, the skilled artisan can readily determine the specific location of the polymorphism given the 3' and 5' nucleotide sequence  
5 flanking the polymorphic site provided in Table 3 and the chromosomal loci information provided herein. The nucleotide sequences of the invention can be double- or single-stranded.

The invention further provides allele-specific oligonucleotides that hybridize to a gene comprising a single nucleotide polymorphism or to the complement of the gene.

10 These oligonucleotides can be probes or primers.

The invention further provides a method of analyzing a nucleic acid from an individual. The method determines which base is present at any one of the polymorphic sites shown in Table 3. Optionally, a set of bases occupying a set of the polymorphic sites shown in Table 3 is determined. This type of analysis can be performed on a  
15 number of individuals, who are tested for the presence of a disease phenotype. The presence or absence of disease phenotype is then correlated with a base or set of bases present at the polymorphic site or sites in the individuals tested.

Thus, the invention further relates to a method of predicting the presence, absence, likelihood of the presence or absence, or severity of a particular phenotype or disorder  
20 associated with a particular genotype. The method comprises obtaining a nucleic acid sample from an individual and determining the identity of one or more bases (nucleotides) at polymorphic sites of genes described herein, wherein the presence of a particular base is correlated with a specified phenotype or disorder, thereby predicting the presence, absence, likelihood of the presence or absence, or severity of the  
25 phenotype or disorder in the individual.

## DEFINITIONS

An oligonucleotide can be DNA or RNA, and single- or double-stranded. Oligonucleotides can be naturally occurring or synthetic, but are typically prepared by

synthetic means. Preferred oligonucleotides of the invention include segments of DNA, or their complements, which include any one of the polymorphic sites shown in Table 3. The segments can be between 5 and 250 bases, and, in specific embodiments, are between 5-10, 5-20, 10-20, 10-50, 20-50 or 10-100 bases. For example, the segment  
 5 can be 21 bases. The polymorphic site can occur within any position of the segment. The segments can be from any of the allelic forms of DNA shown in Table 3.

As used herein, the terms "nucleotide", "base" and "nucleic acid" are intended to be equivalent. The terms "nucleotide sequence", "nucleic acid sequence", "nucleic acid molecule" and "segment" are intended to be equivalent.

10 Hybridization probes are oligonucleotides which bind in a base-specific manner to a complementary strand of nucleic acid. Such probes include peptide nucleic acids, as described in Nielsen *et al.*, *Science* 254, 1497-1500 (1991). Probes can be any length suitable for specific hybridization to the target nucleic acid sequence. The most appropriate length of the probe may vary depending upon the hybridization method in  
 15 which it is being used; for example, particular lengths may be more appropriate for use in microfabricated arrays, while other lengths may be more suitable for use in classical hybridization methods. Such optimizations are known to the skilled artisan. Suitable probes and primers can range from about 5 nucleotides to about 30 nucleotides in length. For example, probes and primers can be 5, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24,  
 20 25, 26, 28 or 30 nucleotides in length. The probe or primer preferably overlaps at least one polymorphic site occupied by any of the possible variant nucleotides. The nucleotide sequence can correspond to the coding sequence of the allele or to the complement of the coding sequence of the allele.

As used herein, the term "primer" refers to a single-stranded oligonucleotide  
 25 which acts as a point of initiation of template-directed DNA synthesis under appropriate conditions (*e.g.*, in the presence of four different nucleoside triphosphates and an agent for polymerization, such as DNA or RNA polymerase or reverse transcriptase) in an appropriate buffer and at a suitable temperature. The appropriate length of a primer depends on the intended use of the primer, but typically ranges from 15 to 30

nucleotides. Short primer molecules generally require cooler temperatures to form sufficiently stable hybrid complexes with the template. A primer need not reflect the exact sequence of the template, but must be sufficiently complementary to hybridize with a template. The term primer site refers to the area of the target DNA to which a primer hybridizes. The term primer pair refers to a set of primers including a 5' (upstream) primer that hybridizes with the 5' end of the DNA sequence to be amplified and a 3' (downstream) primer that hybridizes with the complement of the 3' end of the sequence to be amplified.

As used herein, linkage describes the tendency of genes, alleles, loci or genetic markers to be inherited together as a result of their location on the same chromosome. It can be measured by percent recombination between the two genes, alleles, loci or genetic markers.

As used herein, polymorphism refers to the occurrence of two or more genetically determined alternative sequences or alleles in a population. A polymorphic marker or site is the locus at which divergence occurs. Preferred markers have at least two alleles, each occurring at frequency of greater than 1%, and more preferably greater than 10% or 20% of a selected population. A polymorphic locus may be as small as one base pair. Polymorphic markers include restriction fragment length polymorphisms, variable number of tandem repeats (VNTR's), hypervariable regions, minisatellites, dinucleotide repeats, trinucleotide repeats, tetranucleotide repeats, simple sequence repeats, and insertion elements such as Alu. The first identified allelic form is arbitrarily designated as the reference form and other allelic forms are designated as alternative or variant alleles. The allelic form occurring most frequently in a selected population is sometimes referred to as the wildtype form. Diploid organisms may be homozygous or heterozygous for allelic forms. A diallelic or biallelic polymorphism has two forms. A triallelic polymorphism has three forms.

Work described herein pertains to the resequencing of large numbers of genes in a large number of individuals to identify polymorphisms which can predispose individuals to disease, particularly IBD.

By altering amino acid sequence, SNPs may alter the function of the encoded proteins. The discovery of the SNP facilitates biochemical analysis of the variants and the development of assays to characterize the variants and to screen for pharmaceutical that would interact directly with on or another form of the protein. SNPs (including  
5 silent SNPs) may also alter the regulation of the gene at the transcriptional or post-transcriptional level. SNPs (including silent SNPs) also enable the development of specific DNA, RNA, or protein-based diagnostics that detect the presence or absence of the polymorphism in particular conditions.

A single nucleotide polymorphism occurs at a polymorphic site occupied by a  
10 single nucleotide, which is the site of variation between allelic sequences. The site is usually preceded by and followed by highly conserved sequences of the allele (e.g., sequences that vary in less than 1/100 or 1/1000 members of the populations).

A single nucleotide polymorphism usually arises due to substitution of one nucleotide for another at the polymorphic site. A transition is the replacement of one  
15 purine by another purine or one pyrimidine by another pyrimidine. A transversion is the replacement of a purine by a pyrimidine or vice versa. Single nucleotide polymorphisms can also arise from a deletion of a nucleotide or an insertion of a nucleotide relative to a reference allele. Typically the polymorphic site is occupied by a base other than the reference base. For example, where the reference allele contains the  
20 base "T" at the polymorphic site, the altered allele can contain a "C", "G" or "A" at the polymorphic site.

Hybridizations are usually performed under stringent conditions, for example, at a salt concentration of no more than 1 M and a temperature of at least 25°C. For example, conditions of 5X SSPE (750 mM NaCl, 50 mM NaPhosphate, 5 mM EDTA,  
25 pH 7.4) and a temperature of 25-30°C, or equivalent conditions, are suitable for allele-specific probe hybridizations. Equivalent conditions can be determined by varying one or more of the parameters given as an example, as known in the art, while maintaining a similar degree of identity or similarity between the target nucleotide sequence and the primer or probe used.

The term "isolated" is used herein to indicate that the material in question exists in a physical milieu distinct from that in which it occurs in nature. For example, an isolated nucleic acid of the invention may be substantially isolated with respect to the complex cellular milieu in which it naturally occurs. In some instances, the isolated material will form part of a composition (for example, a crude extract containing other substances), buffer system or reagent mix. In other circumstance, the material may be purified to essential homogeneity, for example as determined by PAGE or column chromatography such as HPLC. Preferably, an isolated nucleic acid comprises at least about 50, 80 or 90 percent (on a molar basis) of all macromolecular species present.

## 10 I. Novel Polymorphisms of the Invention

The novel polymorphisms of the invention are shown in Table 3.

## II. Analysis of Polymorphisms

### A. Preparation of Samples

Polymorphisms are detected in a target nucleic acid from an individual being analyzed. For assay of genomic DNA, virtually any biological sample (other than pure red blood cells) is suitable. For example, convenient tissue samples include whole blood, semen, saliva, tears, urine, fecal material, sweat, buccal, skin and hair. For assay of cDNA or mRNA, the tissue sample must be obtained from an organ in which the target nucleic acid is expressed. For example, if the target nucleic acid is a cytochrome P450, the liver is a suitable source.

Many of the methods described below require amplification of DNA from target samples. This can be accomplished by e.g., PCR. *See generally PCR Technology: Principles and Applications for DNA Amplification* (ed. H.A. Erlich, Freeman Press, NY, NY, 1992); *PCR Protocols: A Guide to Methods and Applications* (eds. Innis, et al., Academic Press, San Diego, CA, 1990); Mattila et al., *Nucleic Acids Res.* 19, 4967 (1991); Eckert et al., *PCR Methods and Applications* 1, 17 (1991); *PCR* (eds. McPherson et al., IRL Press, Oxford); and U.S. Patent 4,683,202.

Other suitable amplification methods include the ligase chain reaction (LCR) (see Wu and Wallace, *Genomics* 4, 560 (1989), Landegren *et al.*, *Science* 241, 1077 (1988), transcription amplification (Kwoh *et al.*, *Proc. Natl. Acad. Sci. USA* 86, 1173 (1989)), and self-sustained sequence replication (Guatelli *et al.*, *Proc. Nat. Acad. Sci. USA*, 87, 1874 (1990)) and nucleic acid based sequence amplification (NASBA). The latter two  
 5 amplification methods involve isothermal reactions based on isothermal transcription, which produce both single stranded RNA (ssRNA) and double stranded DNA (dsDNA) as the amplification products in a ratio of about 30 or 100 to 1, respectively.

#### B. Detection of Polymorphisms in Target DNA

10 The polymorphisms identified as described herein can be used as a platform for genotyping (i.e., determining the genotype of) individuals. This analysis determines which form(s) of a characterized (known) polymorphism are present in individuals under test. There are a variety of suitable procedures, which are discussed in turn.

##### 1. Allele-Specific Probes

15 The design and use of allele-specific probes for analyzing polymorphisms is described by e.g., Saiki *et al.*, *Nature* 324, 163-166 (1986); Dattagupta, EP 235,726, Saiki, WO 89/11548. Allele-specific probes can be designed that hybridize to a segment of target DNA from one individual but do not hybridize to the corresponding segment from another individual due to the presence of different polymorphic forms in  
 20 the respective segments from the two individuals. Hybridization conditions should be sufficiently stringent that there is a significant difference in hybridization intensity between alleles, and preferably an essentially binary response, whereby a probe hybridizes to only one of the alleles. Some probes are designed to hybridize to a segment of target DNA such that the polymorphic site aligns with a central position  
 25 (e.g., in a 15-mer at the 7 position; in a 16-mer, at either the 8 or 9 position) of the probe. This design of probe achieves good discrimination in hybridization between different allelic forms.

Allele-specific probes are often used in pairs, one member of a pair showing a perfect match to a reference form of a target sequence and the other member showing a perfect match to a variant form. Several pairs of probes can then be immobilized on the same support for simultaneous analysis of multiple polymorphisms within the same  
5 target sequence.

## 2. Tiling Arrays

The polymorphisms can also be identified by hybridization to nucleic acid arrays, some examples of which are described in WO 95/11995. One form of such arrays is described in the Examples section in connection with de novo identification of  
10 polymorphisms. The same array or a different array can be used for analysis of characterized polymorphisms. WO 95/11995 also describes subarrays that are optimized for detection of a variant form of a precharacterized polymorphism. Such a subarray contains probes designed to be complementary to a second reference sequence, which is an allelic variant of the first reference sequence. The second group of probes is  
15 designed by the same principles as described in the Examples, except that the probes exhibit complementarity to the second reference sequence. The inclusion of a second group (or further groups) can be particularly useful for analyzing short subsequences of the primary reference sequence in which multiple mutations are expected to occur within a short distance commensurate with the length of the probes (e.g., two or more  
20 mutations within 9 to 21 bases).

## 3. Allele-Specific Primers

An allele-specific primer hybridizes to a site on target DNA overlapping a polymorphism and only primes amplification of an allelic form to which the primer exhibits perfect complementarity. See Gibbs, *Nucleic Acid Res.* 17, 2427-2448 (1989).  
25 This primer is used in conjunction with a second primer which hybridizes at a distal site. Amplification proceeds from the two primers, resulting in a detectable product which indicates the particular allelic form is present. A control is usually performed with a

second pair of primers, one of which shows a single base mismatch at the polymorphic site and the other of which exhibits perfect complementarity to a distal site. The single-base mismatch prevents amplification and no detectable product is formed. The method works best when the mismatch is included in the 3'-most position of the oligonucleotide  
5 aligned with the polymorphism because this position is most destabilizing to elongation from the primer (see, e.g., WO 93/22456).

#### 4. Direct-Sequencing

The direct analysis of the sequence of polymorphisms of the present invention can be accomplished using either the dideoxy chain termination method or the Maxam -  
10 Gilbert method (see Sambrook *et al.*, *Molecular Cloning, A Laboratory Manual* (2nd Ed., CSHP, New York 1989); Zyskind *et al.*, *Recombinant DNA Laboratory Manual*, (Acad. Press, 1988)).

#### 5. Denaturing Gradient Gel Electrophoresis

Amplification products generated using the polymerase chain reaction can be  
15 analyzed by the use of denaturing gradient gel electrophoresis. Different alleles can be identified based on the different sequence-dependent melting properties and electrophoretic migration of DNA in solution. Erlich, ed., *PCR Technology, Principles and Applications for DNA Amplification*, (W.H. Freeman and Co, New York, 1992), Chapter 7.

#### 20 6. Single-Strand Conformation Polymorphism Analysis

Alleles of target sequences can be differentiated using single-strand conformation polymorphism analysis, which identifies base differences by alteration in electrophoretic migration of single stranded PCR products, as described in Orita *et al.*, *Proc. Nat. Acad. Sci.* 86, 2766-2770 (1989). Amplified PCR products can be generated as described  
25 above, and heated or otherwise denatured, to form single stranded amplification products. Single-stranded nucleic acids may refold or form secondary structures which



are partially dependent on the base sequence. The different electrophoretic mobilities of single-stranded amplification products can be related to base-sequence differences between alleles of target sequences.

## 7. Single Base Extension

- 5 An alternative method for identifying and analyzing polymorphisms is based on single-base extension (SBE) of a fluorescently-labeled primer coupled with fluorescence resonance energy transfer (FRET) between the label of the added base and the label of the primer. Typically, the method, such as that described by Chen *et al.*, (*PNAS* 94:10756-61 (1997), incorporated herein by reference) uses a locus-specific
- 10 oligonucleotide primer labeled on the 5' terminus with 5-carboxyfluorescein (FAM). This labeled primer is designed so that the 3' end is immediately adjacent to the polymorphic site of interest. The labeled primer is hybridized to the locus, and single base extension of the labeled primer is performed with fluorescently labeled
- 15 dideoxynucleotides (ddNTPs) in dye-terminator sequencing fashion, except that no deoxyribonucleotides are present. An increase in fluorescence of the added ddNTP in response to excitation at the wavelength of the labeled primer is used to infer the identity of the added nucleotide.

## III. Methods of Use

- After determining polymorphic form(s) present in an individual at one or more
- 20 polymorphic sites, this information can be used in a number of methods.

### A. Forensics

- Determination of which polymorphic forms occupy a set of polymorphic sites in an individual identifies a set of polymorphic forms that distinguishes the individual. *See generally* National Research Council, *The Evaluation of Forensic DNA Evidence* (Eds.
- 25 Pollard *et al.*, National Academy Press, DC, 1996). The more sites that are analyzed, the lower the probability that the set of polymorphic forms in one individual is the same

as that in an unrelated individual. Preferably, if multiple sites are analyzed, the sites are  
 unlinked. Thus, polymorphisms of the invention are often used in conjunction with  
 polymorphisms in distal genes. Preferred polymorphisms for use in forensics are  
 biallelic because the population frequencies of two polymorphic forms can usually be  
 5 determined with greater accuracy than those of multiple polymorphic forms at multi-  
 allelic loci.

The capacity to identify a distinguishing or unique set of forensic markers in an  
 individual is useful for forensic analysis. For example, one can determine whether a  
 blood sample from a suspect matches a blood or other tissue sample from a crime scene  
 10 by determining whether the set of polymorphic forms occupying selected polymorphic  
 sites is the same in the suspect and the sample. If the set of polymorphic markers does  
 not match between a suspect and a sample, it can be concluded (barring experimental  
 error) that the suspect was not the source of the sample. If the set of markers does  
 match, one can conclude that the DNA from the suspect is consistent with that found at  
 15 the crime scene. If frequencies of the polymorphic forms at the loci tested have been  
 determined (e.g., by analysis of a suitable population of individuals), one can perform a  
 statistical analysis to determine the probability that a match of suspect and crime scene  
 sample would occur by chance.

$p(\text{ID})$  is the probability that two random individuals have the same polymorphic or  
 20 allelic form at a given polymorphic site. In biallelic loci, four genotypes are possible:  
 AA, AB, BA, and BB. If alleles A and B occur in a haploid genome of the organism  
 with frequencies  $x$  and  $y$ , the probability of each genotype in a diploid organism is (see  
 WO 95/12607):

Homozygote:  $p(\text{AA}) = x^2$   
 25 Homozygote:  $p(\text{BB}) = y^2 = (1-x)^2$   
 Single Heterozygote:  $p(\text{AB}) = p(\text{BA}) = xy = x(1-x)$   
 Both Heterozygotes:  $p(\text{AB} + \text{BA}) = 2xy = 2x(1-x)$

The probability of identity at one locus (i.e, the probability that two individuals, picked at random from a population will have identical polymorphic forms at a given locus) is given by the equation:

$$p(ID) = (x^2)^2 + (2xy)^2 + (y^2)^2.$$

- 5        These calculations can be extended for any number of polymorphic forms at a given locus. For example, the probability of identity p(ID) for a 3-allele system where the alleles have the frequencies in the population of x, y and z, respectively, is equal to the sum of the squares of the genotype frequencies:

$$p(ID) = x^4 + (2xy)^2 + (2yz)^2 + (2xz)^2 + z^4 + y^4$$

- 10       In a locus of n alleles, the appropriate binomial expansion is used to calculate p(ID) and p(exc).

The cumulative probability of identity (cum p(ID)) for each of multiple unlinked loci is determined by multiplying the probabilities provided by each locus.

$$\text{cum } p(ID) = p(ID1)p(ID2)p(ID3).... p(IDn)$$

- 15       The cumulative probability of non-identity for n loci (i.e. the probability that two random individuals will be different at 1 or more loci) is given by the equation:

$$\text{cum } p(\text{nonID}) = 1-\text{cum } p(ID).$$

If several polymorphic loci are tested, the cumulative probability of non-identity for random individuals becomes very high (e.g., one billion to one). Such probabilities

- 20       can be taken into account together with other evidence in determining the guilt or innocence of the suspect.

B. Paternity Testing

The object of paternity testing is usually to determine whether a male is the father of a child. In most cases, the mother of the child is known and thus, the mother's

- 25       contribution to the child's genotype can be traced. Paternity testing investigates whether the part of the child's genotype not attributable to the mother is consistent with that of

the putative father. Paternity testing can be performed by analyzing sets of polymorphisms in the putative father and the child.

If the set of polymorphisms in the child attributable to the father does not match the set of polymorphisms of the putative father, it can be concluded, barring  
 5 experimental error, that the putative father is not the real father. If the set of polymorphisms in the child attributable to the father does match the set of polymorphisms of the putative father, a statistical calculation can be performed to determine the probability of coincidental match.

The probability of parentage exclusion (representing the probability that a random  
 10 male will have a polymorphic form at a given polymorphic site that makes him incompatible as the father) is given by the equation (see WO 95/12607):

$$p(\text{exc}) = xy(1-xy)$$

where x and y are the population frequencies of alleles A and B of a biallelic polymorphic site.

15 (At a triallelic site  $p(\text{exc}) = xy(1-xy) + yz(1-yz) + xz(1-xz) + 3xyz(1-xyz)$ ), where x, y and z are the respective population frequencies of alleles A, B and C).

The probability of non-exclusion is

$$p(\text{non-exc}) = 1 - p(\text{exc})$$

The cumulative probability of non-exclusion (representing the value obtained  
 20 when n loci are used) is thus:

$$\text{cum } p(\text{non-exc}) = p(\text{non-exc1})p(\text{non-exc2})p(\text{non-exc3})\dots p(\text{non-excn})$$

The cumulative probability of exclusion for n loci (representing the probability that a random male will be excluded)

$$\text{cum } p(\text{exc}) = 1 - \text{cum } p(\text{non-exc}).$$

25 If several polymorphic loci are included in the analysis, the cumulative probability of exclusion of a random male is very high. This probability can be taken into account in assessing the liability of a putative father whose polymorphic marker set matches the child's polymorphic marker set attributable to his/her father.

C. Correlation of Polymorphisms with Phenotypic Traits

The polymorphisms of the invention may contribute to the phenotype of an organism in different ways. Some polymorphisms occur within a protein coding sequence and contribute to phenotype by affecting protein structure. The effect may be neutral, beneficial or detrimental, or both beneficial and detrimental, depending on the circumstances. For example, a heterozygous sickle cell mutation confers resistance to malaria, but a homozygous sickle cell mutation is usually lethal. Other polymorphisms occur in noncoding regions but may exert phenotypic effects indirectly via influence on replication, transcription, and translation. A single polymorphism may affect more than one phenotypic trait. Likewise, a single phenotypic trait may be affected by polymorphisms in different genes. Further, some polymorphisms predispose an individual to a distinct mutation that is causally related to a certain phenotype. For example, the polymorphisms identified herein and shown in Table 3 are present in the chromosomal loci which have been identified as described herein as conferring susceptibility to IBD such as CD and UC.

Correlation is performed for a population of individuals who have been tested for the presence or absence of a phenotypic trait of interest and for polymorphic markers sets. To perform such analysis, the presence or absence of a set of polymorphisms (i.e. a polymorphic set) is determined for a set of the individuals, some of whom exhibit a particular trait, and some of which exhibit lack of the trait. The alleles of each polymorphism of the set are then reviewed to determine whether the presence or absence of a particular allele is associated with the trait of interest. Correlation can be performed by standard statistical methods such as a  $\kappa$ -squared test and statistically significant correlations between polymorphic form(s) and phenotypic characteristics are noted. For example, it might be found that the presence of allele A1 at polymorphism A correlates with heart disease. As a further example, it might be found that the combined presence of allele A1 at polymorphism A and allele B1 at polymorphism B correlates with increased susceptibility to IBD (e.g., CD and UC).

Such correlations can be exploited in several ways. In the case of a strong correlation between a set of one or more polymorphic forms and a disease for which treatment is available, detection of the polymorphic form set in a human or animal patient may justify immediate administration of treatment, or at least the institution of

5 regular monitoring of the patient. Detection of a polymorphic form correlated with serious disease in a couple contemplating a family may also be valuable to the couple in their reproductive decisions. For example, the female partner might elect to undergo *in vitro* fertilization to avoid the possibility of transmitting such a polymorphism from her husband to her offspring. In the case of a weaker, but still statistically significant

10 correlation between a polymorphic set and human disease, immediate therapeutic intervention or monitoring may not be justified. Nevertheless, the patient can be motivated to begin simple life-style changes (e.g., diet, exercise) that can be accomplished at little cost to the patient but confer potential benefits in reducing the risk of conditions to which the patient may have increased susceptibility by virtue of variant

15 alleles. Identification of a polymorphic set in a patient correlated with enhanced receptiveness to one of several treatment regimes for a disease indicates that this treatment regime should be followed.

For animals and plants, correlations between characteristics and phenotype are useful for breeding for desired characteristics. For example, Beitz *et al.*, US 5,292,639

20 discuss use of bovine mitochondrial polymorphisms in a breeding program to improve milk production in cows. To evaluate the effect of mtDNA D-loop sequence polymorphism on milk production, each cow was assigned a value of 1 if variant or 0 if wildtype with respect to a prototypical mitochondrial DNA sequence at each of 17

locations considered. Each production trait was analyzed individually with the

25 following animal model:

$$Y_{ijkpn} = \mu + YS_i + P_j + X_k + \beta_1 + \dots \beta_{17} + PE_n + a_n + e_p$$

where  $Y_{ijkpn}$  is the milk, fat, fat percentage, SNF, SNF percentage, energy concentration, or lactation energy record;  $\mu$  is an overall mean;  $YS_i$  is the effect common to all cows calving in year-season;  $X_k$  is the effect common to cows in either the high or average

selection line;  $\beta_1$  to  $\beta_{17}$  are the binomial regressions of production record on mtDNA D-loop sequence polymorphisms;  $PE_n$  is permanent environmental effect common to all records of cow  $n$ ;  $a_n$  is effect of animal  $n$  and is composed of the additive genetic contribution of sire and dam breeding values and a Mendelian sampling effect; and  $e_p$  is a random residual. It was found that eleven of seventeen polymorphisms tested influenced at least one production trait. Bovines having the best polymorphic forms for milk production at these eleven loci are used as parents for breeding the next generation of the herd.

D. Genetic Mapping of Phenotypic Traits

The previous section concerns identifying correlations between phenotypic traits (e.g., IBD) and polymorphisms that directly or indirectly contribute to those traits, such as those identified in Table 3. The present section describes identification of a physical linkage between a genetic locus associated with a trait of interest and polymorphic markers that are not associated with the trait, but are in physical proximity with the genetic locus responsible for the trait and co-segregate with it. Such analysis is useful for mapping a genetic locus associated with a phenotypic trait to a chromosomal position, and thereby cloning gene(s) responsible for the trait. See Lander *et al.*, *Proc. Natl. Acad. Sci. (USA)* 83, 7353-7357 (1986); Lander *et al.*, *Proc. Natl. Acad. Sci. (USA)* 84, 2363-2367 (1987); Donis-Keller *et al.*, *Cell* 51, 319-337 (1987); Lander *et al.*, *Genetics* 121, 185-199 (1989)). Genes localized by linkage can be cloned by a process known as directional cloning. See Wainwright, *Med. J. Australia* 159, 170-174 (1993); Collins, *Nature Genetics* 1, 3-6 (1992).

Linkage studies are typically performed on members of a family. Available members of the family are characterized for the presence or absence of a phenotypic trait and for a set of polymorphic markers. The distribution of polymorphic markers in an informative meiosis is then analyzed to determine which polymorphic markers co-segregate with a phenotypic trait. See, e.g., Kerem *et al.*, *Science* 245, 1073-1080

(1989); Monaco *et al.*, *Nature* 316, 842 (1985); Yamoka *et al.*, *Neurology* 40, 222-226 (1990); Rossiter *et al.*, *FASEB Journal* 5, 21-27 (1991).

Linkage is analyzed by calculation of LOD (log of the odds) values. A lod value is the relative likelihood of obtaining observed segregation data for a marker and a genetic locus when the two are located at a recombination fraction  $\theta$ , versus the situation in which the two are not linked, and thus segregating independently (Thompson & Thompson, *Genetics in Medicine* (5th ed, W.B. Saunders Company, Philadelphia, 1991); Strachan, "Mapping the human genome" in *The Human Genome* (BIOS Scientific Publishers Ltd, Oxford), Chapter 4). A series of likelihood ratios are calculated at various recombination fractions ( $\theta$ ), ranging from  $\theta = 0.0$  (coincident loci) to  $\theta = 0.50$  (unlinked). Thus, the likelihood at a given value of  $\theta$  is: probability of data if loci linked at  $\theta$  to probability of data if loci unlinked. The computed likelihoods are usually expressed as the  $\log_{10}$  of this ratio (i.e., a lod score). For example, a lod score of 3 indicates 1000:1 odds against an apparent observed linkage being a coincidence.

The use of logarithms allows data collected from different families to be combined by simple addition. Computer programs are available for the calculation of lod scores for differing values of  $\theta$  (e.g., LIPED, MLINK (Lathrop, *Proc. Nat. Acad. Sci. (USA)* 81, 3443-3446 (1984)). For any particular lod score, a recombination fraction may be determined from mathematical tables. See Smith *et al.*, *Mathematical tables for research workers in human genetics* (Churchill, London, 1961); Smith, *Ann. Hum. Genet.* 32, 127-150 (1968). The value of  $\theta$  at which the lod score is the highest is considered to be the best estimate of the recombination fraction.

Positive lod score values suggest that the two loci are linked, whereas negative values suggest that linkage is less likely (at that value of  $\theta$ ) than the possibility that the two loci are unlinked. By convention, a combined lod score of +3 or greater (equivalent to greater than 1000:1 odds in favor of linkage) is considered definitive evidence that two loci are linked. Similarly, by convention, a negative lod score of -2 or less is taken as definitive evidence against linkage of the two loci being compared. Negative linkage



data are useful in excluding a chromosome or a segment thereof from consideration. The search focuses on the remaining non-excluded chromosomal locations.

#### IV. Modified Polypeptides and Gene Sequences

The invention further provides variant forms of nucleic acids and corresponding  
 5 proteins. The nucleic acids comprise one of the sequences described in Table 3, in which the polymorphic position is occupied by one of the alternative bases for that position. Some nucleic acids encode full-length variant forms of proteins. Similarly, variant proteins have the prototypical amino acid sequences encoded by nucleic acid sequences shown in Table 3, (read so as to be in-frame with the full-length coding  
 10 sequence of which it is a component) except at an amino acid encoded by a codon including one of the polymorphic positions shown in Table 3. That position is occupied by the amino acid coded by the corresponding codon in any of the alternative forms shown in Table 3.

Variant genes can be expressed in an expression vector in which a variant gene is  
 15 operably linked to a native or other promoter. Usually, the promoter is a eukaryotic promoter for expression in a mammalian cell. The transcription regulation sequences typically include a heterologous promoter and optionally an enhancer which is recognized by the host. The selection of an appropriate promoter, for example trp, lac, phage promoters, glycolytic enzyme promoters and tRNA promoters, depends on the  
 20 host selected. Commercially available expression vectors can be used. Vectors can include host-recognized replication systems, amplifiable genes, selectable markers, host sequences useful for insertion into the host genome, and the like.

The means of introducing the expression construct into a host cell varies depending upon the particular construction and the target host. Suitable means include  
 25 fusion, conjugation, transfection, transduction, electroporation or injection, as described in Sambrook, *supra*. A wide variety of host cells can be employed for expression of the variant gene, both prokaryotic and eukaryotic. Suitable host cells include bacteria such as *E. coli*, yeast, filamentous fungi, insect cells, mammalian cells, typically

immortalized, *e.g.*, mouse, CHO, human and monkey cell lines and derivatives thereof. Preferred host cells are able to process the variant gene product to produce an appropriate mature polypeptide. Processing includes glycosylation, ubiquitination, disulfide bond formation, general post-translational modification, and the like. As used  
5 herein, "gene product" includes mRNA, peptide and protein products.

The protein may be isolated by conventional means of protein biochemistry and purification to obtain a substantially pure product, *i.e.*, 80, 95 or 99% free of cell component contaminants, as described in Jacoby, *Methods in Enzymology* Volume 104, Academic Press, New York (1984); Scopes, *Protein Purification, Principles and*  
10 *Practice*, 2nd Edition, Springer-Verlag, New York (1987); and Deutscher (ed), *Guide to Protein Purification, Methods in Enzymology*, Vol. 182 (1990). If the protein is secreted, it can be isolated from the supernatant in which the host cell is grown. If not secreted, the protein can be isolated from a lysate of the host cells.

The invention further provides transgenic nonhuman animals capable of  
15 expressing an exogenous variant gene and/or having one or both alleles of an endogenous variant gene inactivated. Expression of an exogenous variant gene is usually achieved by operably linking the gene to a promoter and optionally an enhancer, and microinjecting the construct into a zygote. *See* Hogan *et al.*, "Manipulating the Mouse Embryo, A Laboratory Manual," Cold Spring Harbor Laboratory. Inactivation  
20 of endogenous variant genes can be achieved by forming a transgene in which a cloned variant gene is inactivated by insertion of a positive selection marker. *See* Capecchi, *Science* 244, 1288-1292 (1989). The transgene is then introduced into an embryonic stem cell, where it undergoes homologous recombination with an endogenous variant gene. Mice and other rodents are preferred animals. Such animals provide useful drug  
25 screening systems.

In addition to substantially full-length polypeptides expressed by variant genes, the present invention includes biologically active fragments of the polypeptides, or analogs thereof, including organic molecules which simulate the interactions of the peptides. Biologically active fragments include any portion of the full-length

polypeptide which confers a biological function on the variant gene product, including ligand binding, and antibody binding. Ligand binding includes binding by nucleic acids, proteins or polypeptides, small biologically active molecules, or large cellular structures.

Polyclonal and/or monoclonal antibodies that specifically bind to variant gene products but not to corresponding prototypical gene products are also provided.

Antibodies can be made by injecting mice or other animals with the variant gene product or synthetic peptide fragments thereof. Monoclonal antibodies are screened as are described, for example, in Harlow & Lane, *Antibodies, A Laboratory Manual*, Cold Spring Harbor Press, New York (1988); Goding, *Monoclonal antibodies, Principles and Practice* (2d ed.) Academic Press, New York (1986). Monoclonal antibodies are tested for specific immunoreactivity with a variant gene product and lack of immunoreactivity to the corresponding prototypical gene product. These antibodies are useful in diagnostic assays for detection of the variant form, or as an active ingredient in a pharmaceutical composition.

## 15 V. Kits

The invention further provides kits comprising at least one allele-specific oligonucleotide as described herein. Often, the kits contain one or more pairs of allele-specific oligonucleotides hybridizing to different forms of a polymorphism. In some kits, the allele-specific oligonucleotides are provided immobilized to a substrate. For example, the same substrate can comprise allele-specific oligonucleotide probes for detecting at least 10, 100 or all of the polymorphisms shown in Table 3. Optional additional components of the kit include, for example, restriction enzymes, reverse-transcriptase or polymerase, the substrate nucleoside triphosphates, means used to label (for example, an avidin-enzyme conjugate and enzyme substrate and chromogen if the label is biotin), and the appropriate buffers for reverse transcription, PCR, or hybridization reactions. Usually, the kit also contains instructions for carrying out the methods.

The following Examples are offered for the purpose of illustrating the present invention and are not to be construed to limit the scope of this invention. The teachings of all references cited herein are hereby incorporated herein by reference.

### EXAMPLES

5        With the goal of identifying IBD susceptibility genes, a genomewide scan was undertaken in 163 pedigrees, and three regions of suggestive linkage (3, 5q31-33, 6p) and one of significant linkage to 19p13 (LOD = 4.6) were identified. Higher density mapping in the suggestive 5q31-33 region revealed a CD susceptibility locus of genome-wide significance (LOD = 3.9). Importantly, the 5q31-p33 localizes to the  
10    major immunoregulatory cytokine gene cluster and the 19p13 locus to a region containing numerous genes encoding cytokine/chemokine receptors and other inflammatory-associated molecules that could have a direct role in disease susceptibility.

      In order to pursue the evidence of linkage to chromosome 5, a systematic linkage  
15    disequilibrium (LD) approach was adopted. The approach that was used in the first stage of LD mapping was to genotype all known microsatellite markers in the 18 cM between D5S1435 and D5S1480, as these two markers delimit a region of a 2 LOD drop on either side of the linkage peak centered at marker D5S2497. All alleles for each marker were examined for evidence of excess transmission from heterozygous parents  
20    to CD child using the transmission disequilibrium test (TDT). Only alleles at two of the 57 markers had significant  $C^2$  results ( $p < 0.001$ ): IRF1p1 ( $C^2 = 13.3$ ,  $p = 0.0003$ ) and D5S1984 ( $C^2 = 14.0$ ,  $p = 0.0002$ ) (Table 1). A second stage of mapping was then undertaken to confirm, as well as to better delimit, the region of LD surrounding IRF1p1 and D5S1984. The development of new microsatellite markers was necessary.  
25    The marker with the most significant  $C^2$  result was CAh17a ( $C^2 = 16.2$ ,  $p = 0.00006$ ) and was located between IRF1p1 and D5S1984 (Table 2). Furthermore, the alleles 193, 156, 373, 140, 222, and 307 at markers GAh18a, IRF1p, CAh15a, CAh17a, D5S1984, CSF2p10, respectively, define a haplotype conferring susceptibility to Crohn's disease

(CD). In order to identify the sequence variant that would explain the genetic susceptibility to CD provided by this haplotype, a search was performed for all single nucleotide polymorphisms (SNPs) in this region of LD. The SNP discovery was accomplished by direct sequencing of overlapping PCR products amplified from DNA samples from eight individuals (six CD patients, one unaffected family member, and one CEPH DNA as control). Table 3 shows the results of the SNP discovery analyses.

139 triads were genotyped for a total of 241 SNPs thus far, where at least 50 trios were fully genotyped. Using a  $C^2$  value of 13 (corresponding to a p-value of 0.05) as threshold, 12 SNPs were found to have a significant level of association with CD and extended over a region of 250 kb, from IRF1 to prolyl4 hydroxylase. These were markers IGR2055a\_1, IGR2060a\_1, IGR2063b\_1, IGR2069a\_2, IGR2078a\_1, IGR2096a\_1, IGR2198a\_1, IGR2230a\_1, IGR2277a\_1, IGR3081a\_1, IGR3096a\_1, PROLYLex3\_1 (see Table 4). Any of these best SNPs by themselves are in strong association with CD and fully explain the microsatellite LD observations. Furthermore, the best SNPs have nearly identical association characteristics (that is, the allele at one SNP determines the allele of all others on any phased chromosome), confirming that a single risk haplotype extending approximately 250 kb is the source of all the observations of association in this region. Specifically, this haplotype is defined by the alleles G, C, G, T, A, A, G, T, G, G, C, T at markers IGR2055a\_1, IGR2060a\_1, IGR2063b\_1, IGR2069a\_2, IGR2078a\_1, IGR2096a\_1, IGR2198a\_1, IGR2230a\_1, IGR2277a\_1, IGR3081a\_1, IGR3096a\_1, PROLYLex3\_1, respectively. The frequency of this haplotype is estimated to be approximately 37% in the general population. Furthermore, this haplotype is transmitted from heterozygous parents to CD patients at a ratio of 2.5:1.

**Families**

For the linkage study, multicase families with 2 or more siblings affected by IBD were identified by review of clinical charts of all patients registered in the Mount Sinai

Hospital Inflammatory Bowel Disease Unit patient database and from the Hospital for Sick Children IBD database. Patients were also referred by physicians in the Greater Toronto Area (GTA). To confirm and update information obtained from these records, all patients were sent a questionnaire inquiring about the presence of a family history of IBD. Individuals identified as having other affected first-degree relatives were invited to participate and asked for permission to contact other affected and unaffected family members. Endoscopic, histological and radiological reports as well as clinical data were obtained on all affected individuals and these reports were reviewed for verification of diagnosis based upon standard criteria. Venous blood sampling was performed on affected individuals and their parents, and DNA was extracted using a salting out procedure. Ethics approval for this study was given by the University of Toronto Ethics Committee and written informed consent was obtained from all participants.

All of the LD analyses in this study were performed with father-mother-affected child (CD only) triads, where 0 or 1 of the parents was affected with CD. These triads either came from the multicase families used in the linkage stage of this study or were identified specifically for the purpose of the LD study. Specifically, for the microsatellite genotyping, 296 triads were genotyped: 95 of these triads were derived from families used in the original identification of the IBD5 locus (only one triad per family), and 201 were from newly collected families. For the SNP genotyping, 139 triads were genotyped: 18 were derived from families used in the original identification of the IBD5 locus, and 121 were from the newly collected families. Individuals affected by CD were identified by review of the clinical charts of all patients registered in the Mount Sinai Hospital Inflammatory Bowel Disease Centre patient database and from the Toronto Hospital for Sick Children IBD database. Written informed consent was obtained from all participants and ethics approval for this study was granted by the University of Toronto Ethics Committee.

### Microsatellite Genotyping

Genomic DNA was extracted from peripheral blood lymphocytes from probands and family members from 163 Caucasian pedigrees. The genome-wide scan, with an average inter-marker spacing of 12 cM, was carried out using a modified version of the

5 Cooperative Human Linkage Centre (CHLC) Screening Set/version 6.0 that also included Genethon markers. These 312 loci were amplified using fluorescently-labeled primers (Research Genetics Inc., Huntsville AL) in

separate polymerase chain reactions, and the products were then multiplexed into panels by pooling before electrophoresis on ABI 377 sequencers (PE Applied Biosystems,

10 Foster City, CA). Fluorescent genotyping gels were analyzed in an automated system developed at the Whitehead Institute/MIT Center for Genome Research. Further details of the genotyping system have previously been described (Rioux *et al.*, *Gastroenterology* 115:1062-1065 (1998)).

The region of suggestive linkage on chromosome 5 and the surrounding regions of

15 poor information content were followed up with 34 additional microsatellite markers. Specifically, 34 markers were genotyped between markers D5S1470 and D5S1471, decreasing the average spacing between markers to approximately 3 cM in this 125 cM region. This higher density mapping was performed on the original samples and on additional 12 families, for a total of 175

20 pedigrees analyzed. These new families consisted of 16 CD affected sibpairs.

In the first phase of the microsatellite LD mapping, a total of 57 microsatellite markers were genotyped on 296 CD triads. Information regarding primer sequence, allele size range, and suggested amplification conditions for 55 of these genetic markers (all but IRF1p1 and CSF2p10) can be obtained from the Genethon

25 (<http://www.genethon.fr/>), Marshfield (<http://research.marshfieldclinic.org/genetics/>), or Genome Database (<http://www.genethon.fr/>) World Wide Web sites. The markers IRF1p1, CSF2p1, and the 8 markers used in the 2nd stage of LD mapping, were designed during the course of this study. Genotypes for all of these markers were obtained as described above.

**SNP Discovery**

In order to identify all SNPs in the *IBD5* critical region, a tiling path of overlapping PCR products was designed. Specifically, PCR assays were designed using Primer 3.0 to be approximately 700 bp in length, with 100 bp overlap with adjacent assays. The -21 M13 forward and the -28 M13 reverse sequences were added to each of the forward and reverse PCR primers, respectively. These PCR primers were used to amplify 50 ng of genomic DNA from six CD patients, one unaffected family member, and one CEPH DNA as control. The PCR products were purified using the solid phase reversible immobilization (SPRI) method and then sequenced using the appropriate -21 M13 or -28 M13 DYEnamic Direct Cycle Sequencing kit (Amersham Pharmacia Biotech Ltd, Cleveland, OH). All sequencing reactions were run on ABI377 automated sequencers (PE Applied BioSystems, Foster City, CA); the gel files were processed using the BASS software, available on the Whitehead Institute/MIT Center for Genome Research FTP site. Sequences were base-called by the Phred program, and then the forward and reverse reads were assembled by the Phrap program. All traces were visually inspected by at least two observers.

**SNP genotyping**

SNP genotyping was performed using length-multiplexed single-base extension (LM-SBE) as previously described. Briefly, PCR primers were designed as close as possible to the SNPs identified in the current study, resulting in a product of a maximum length of 150 bp. Forward primers had T7 tails at their 5' ends and reverse primers had T3 tails at their 5' ends. These T7 and T3 tails were used for secondary amplification. Primer pairs were checked for homology to all amplicons and sorted into pools consisting of up to 50 primer pairs. Loci were subjected to two rounds of PCR amplification. In the first round, 10 ng of genomic DNA was amplified using a pool of primer pairs (0.1 mM) and 2.5 units of Amplitaq Gold (Perkin Elmer). In the second round, a 3 mL aliquot of the primary amplification product was amplified with biotinylated-T7 and biotinylated-T3 primers. A 7 mL aliquot of this secondary



amplification product was purified from the unincorporated dNTPs using streptavidin-coated Dynabeads (Dynal). A multiplex SBE reaction was then carried out on the purified product using SNP-specific primers, JOE-ddATP (0.12 M), TAMRA-ddCTP (0.12 M), FAM-ddGTP (0.12 M), ROX-ddUTP (0.60 M; NEN DuPont) and

5 Thermosequenase (0.5 U; Amersham). Excess ddNTPs were removed from the SBE products using 96-well gel filtration blocks (Edge Biosystems) prior to electrophoresis on ABI 377 sequencers. The SBE gels were analyzed using a system developed at the Whitehead Institute/MIT Center for Genome Research as previously described.

**Statistical analysis**

10 Nonparametric multipoint linkage analysis of the data from the genome-wide scan and the higher density mapping on chromosome 5 was performed using the MAPMAKER/SIBS functions implemented in GENHUNTER 2.0. It is important to note that all sib pairs from sibships with more than 2 affecteds were counted but were conservatively downweighted by a factor of 2/n (where n = the number of affecteds).

15 Exclusion mapping was also performed with this software package, and a locus 8s > 2 was considered excluded at a LOD score of -2.

To establish appropriate thresholds for suggestive and significant genome-wide linkage for these particular datasets, simulations were performed by generating artificial genotype data with the identical family structures. These simulations matched the

20 datasets with respect to marker density, marker informativeness, the individuals genotyped, affected status, and the fraction of missing data.

To assess the significance of the TDT results for each marker, permutation tests using the same genotype data were carried out. For each trio, chromosomes were randomly reassigned as transmitted or untransmitted to form a permuted dataset. The

25 number of permuted datasets with values as significant as that seen for the best single-marker and two-marker tests were tabulated. In order to quantify the extent of LD in the *IBD5* region, 3-marker haplotypes were examined using the TDT and  $P_{\text{excess}}$

(d).  $P_{\text{excess}}$  represents the strength of LD and is calculated by  $(p_{\text{affected}} - p_{\text{normal}}) / (1$

-  $p_{\text{normal}}$ ). In our study, the  $P_{\text{affected}}$  is calculated from the frequency of the haplotype among the transmitted parental chromosomes and  $P_{\text{normal}}$  is the frequency among untransmitted parental chromosomes.

genotype, which is the same as the one used in the previous study. The results of the analysis are shown in Table 1. The results of the analysis are shown in Table 1.

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Table 1. Summary of the first stage of LD mapping using microsatellite markers.

	Marker #	Marker Name	Source of marker	Estimated Genetic Position <sup>2</sup>	Distance to next marker	Previous linkage results (MLOD) <sup>3</sup>		TDT results <sup>4</sup>	
			marker <sub>1</sub>	Position <sup>2</sup>	marker	results (MLOD) <sup>3</sup>	Allele	X <sup>2</sup>	pvalue
5	1	D5S1435	G	128.50	0.50	0.76	115	5.84	0.016
	2	AFMa113ye9	G	129.00	0.83		-	-	-
	3	D5S1505	M	129.83	0.00	0.79	-	-	-
	4	D5S1384	U	129.83	0.00		-	-	-
10	5	D5S471	G	129.83	0.57	0.79	238	7.58	0.0059
	6	D5S632	G	130.40	0.20		114	4.59	0.032
	7	D5S818	M	130.60	0.20		-	-	-
	8	D5S2502	M	130.80	0.10		-	-	-
15	9	AFMB352XH5	G	130.90	0.04		-	-	-
	10	D5S1975	G	130.94	0.00		-	-	-
	11	D5S622	G	130.94	1.86		-	-	-
	12	D5S2059	G	132.80	0.85		190	5.83	0.016
20	13	D5S615	U	133.65	0.00	1.8	-	-	-
	14	D5S804	M	133.65	0.00	1.8	-	-	-
	15	D5S1495	M	133.65	0.00	1.8	382	4.00	0.045
	16	GATA68A03	M	133.65	0.35	2.2	-	-	-
25	17	D5S809	M	134.00	0.40	2.1	-	-	-
	18	D5S2120	G	134.40	0.20		-	-	-
	19	D5S642	G	134.60	0.65	2.6	-	-	-
	20	D5S2057	G	135.25	0.00	3.1	-	-	-
30	21	D5S2110	G	135.25	0.62	3.1	-	-	-
	22	IRF1p1	S	135.87	0.19		156	13.27	0.00027
	23	D5S1984	G	136.06	0.16		222	14.04	0.00018
	24	CSF2p10	S	136.22	0.58		307	4.00	0.045
35	25	D5S2497	G	136.80	0.10	3.9	129	7.69	0.0055
	26	w2429/240wa7	G	136.90	0.10		-	-	-
	27	w866/057vg5	G	137.00	0.10		-	-	-
	28	D5S1766	U	137.10	0.10	3.5	245	6.48	0.011
40	29	D5S808	M	137.20	0.10	3.3	-	-	-
	30	D5S458	G	137.30	0.00	3.1	-	-	-
	31	D5S396	G	137.30	0.09		-	-	-
	32	D5S2053	G	137.39	0.56	3.0	-	-	-
45	33	D5S1995	G	137.95	0.69	2.8	-	-	-
	34	D5S2115	G	138.64	0.68	2.4	-	-	-
	35	IL9	M	139.32	0.01	2.0	-	-	-
	36	D5S816	M	139.33	0.07	2.0	-	-	-
	37	D5S393	G	139.40	0.10	2.0	-	-	-
	38	D5S399	G	139.50	0.90	2.0	127	4.57	0.032
	39	D5S479	G	140.40	0.10		-	-	-
	40	AFM350yb1	G	140.50	0.10		-	-	-
	41	D5S1983	G	140.60	0.12		116	4.55	0.033
	42	D5S476	G	140.72	0.00	1.7	-	-	-
	43	D5S500	G	140.72	0.28	1.7	211	4.15	0.042
	44	AFMB290YC9	G	141.00	0.82		-	-	-
	45	D5S414	G	141.82	0.98		-	-	-

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46	D5S2009	G	142.80	0.12		140	6.70	0.01
47	D5S658	G	142.92	0.00	2.0	-	-	-
48	D5S2116	G	142.92	1.08		-	-	-
49	D5S2011	G	144.00	0.06		-	-	-
50	D5S2119	G	144.06	0.00		-	-	-
51	D5S1979	G	144.06	1.15		-	-	-
52	D5S2017	G	145.21	2.19	2.2	91	5.40	0.02
53	D5S2859	M	147.40	0.09		-	-	-
54	D5S436	G	147.49	0.00	1.6	-	-	-
55	D5S207	M	147.49	0.00		-	-	-
56	D5S1480	M	147.49		1.6	-	-	-

- 15
- <sup>1</sup> Abbreviations: G, Genethon; M, Marshfield; U, Utah; S, designed by authors from genomic sequence.

<sup>2</sup> Estimated from genetic (Genethon, Marshfield) and physical (data not shown) map information

<sup>3</sup> Linkage data for the CD subgroup with early onset disease as seen in figure 1 and reference ###

<sup>4</sup> Results are shown only if pvalue < 0.05

Table 2. Summary of combined LD mapping information.

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Marker #	Marker Name	Distance to next marker (kb)	LD mapping stage	Allele	T:U	TDT results X <sup>2</sup>	pvalue
57	CAh14b	43	2	-		-	-
58	ATTh14c	167	2	-		-	-
59	IL4m2	164	2	214	1.8	4.74	0.029
60	GAh18a	21	2	193	1.4		0.018
22	IRF1p1	24	1	156	1.7	13.27	0.00027
61	CAh15a	130	2	373	1.5	7.73	0.0054
62	CAh17a	97	2	140	1.8	16.19	0.00005
23	D5S1984	163	1	222	1.8	14.04	0.00018
24	CSF2p10	178	1	307	1.4	4.00	0.045
63	CAh81b	85	2	-		-	-
64	CAh81c		2	-		-	-

TABLE 3  
Genomic regions predicted from genomic sequence using the GENSCAN package

Legend:	EST:	expressed sequence tag							
	gene:	known gene							
Predicted gene:	ins/del:	gene predicted from genomic sequence using the GENSCAN package							
	genomic:	insertion/deletion							
		derived from resequencing of entire genomic region (therefore includes genes, promoters, enhancers, etc.)							
Notes:	1)	"N" in sequence represents polymorphic base							
	2)	details are provided where currently available							
	3)	This list includes all polymorphisms: SNPs, repeats, and insertions/deletions							
Polymorphism	Poly	comment #1	comment #2	comment #3	comment #4	Gene Name	Flanking Sequence		
Name	type	Polymorphisms details	Verification		Position on reference genomic sequence (attached)				
			Status						
1 CSF2_6610	c/t		Verified	gene	n/a	colony stimulating factor 2	aaactctctgtgcaaccacagatcatcaccttggaaa gtttcaaaag		
2 CSFenh_1492	g/t		Verified	gene	n/a	colony stimulating factor 2 (enhancer)	atttctcccttggataatgtctctctgtNataagga tctggagtgactcaagc		
3 CSFenh_1580	g/t		Verified	gene	n/a	colony stimulating factor 2 (enhancer)	acacgcataaggaaaactctctccagaggggtttcNc ctgtctctgtaggaaagggggcccccagaggg		
4 CSFex4_6632	c/t		Verified	gene	n/a	colony stimulating factor 2	aaaggaaactctctgtgcaaccacagatcatcacct tgaaaagtttcaaaagaga		
5 E4ex1_1	t/c		Verified	EST	n/a	n/a	ctgggaaccacaaacatctctggagaaNagctgag aacctaccaaggga		
6 E4ex1_2	a/g		Verified	EST	n/a	n/a	agacagaaaaattagcttagagatggagggtggca Ngatctaaagctgtccctccgctgcc		
7 E4ex1_3	t/c		Verified	EST	n/a	n/a	atgggagggtggcac- gatctctaaagctgtccNgtgtccattcaggaggtgc ctcatgcataag		
8 Facorex16_1	g/c		Verified	gene	n/a	Fatty acid CoA ligase	ggctacttgaaaagatccacagacaggatNgaaggag gccctggacagcgtatggc		

9	FaCoex1_1	t/c	Verified	gene	n/a	Fatty acid CoA ligase	accaggaggagcctgtctaccaccctgctaaNggctct accaccaccggcttctc
10	GENS010ex2_1	t/c	Verified	Predicted gene	n/a		agaagcagtagggcNactactaggtagcccca
11	GENS020ex1_1	a/g	Verified	Predicted gene	n/a		gggtgtgacagaggctgNtggcaggactc
12	GENS020ex3_1	a/c	Verified	Predicted gene	n/a		ggcgccacNcaaaactctgcgcagtc
13	GENS020ex3_2	t/g	Verified	Predicted gene	n/a		aggccagccctNttcctactatgtct
14	GENS020ex3_3	a/g	Verified	Predicted gene	n/a		tagaagcagaaggtgtgtggcctcNcigtgtg ggacttctgccacacgcac
15	GENS021ex1_1	g/c	Verified	Predicted gene	n/a		tcatggcgggtgtctgtgacctgagagaggNtca gatggaagaagcctgggtgaggaatgag
16	GENS021ex1_2	t/c	Verified	Predicted gene	n/a		aaggccctcatgtatcatgattaNgtgtgtgtgtg tccatgcct
17	GENS025ex1_1	a/g	Verified	Predicted gene	n/a		gctccaagccctggggagggaagtggtg acccac
18	GENS026ex12_1	a/t	Verified	Predicted gene	n/a		ctttcatgtagaagagctagtagtactgtattNtata atgcttaccatgtccatatagaacaagctcc
19	GENS026ex3_1	t/c	Verified	Predicted gene	n/a		tccttcacacaaacacctaaagtaaccNagagca ataggactcctgtlaaa
20	GENS026ex4_1	t/c	Verified	Predicted gene	n/a		gggtttgtgtatctaaaaataggNgacctcagcctta aaacctcatct
21	GENS026ex5_1	t/c	Verified	Predicted gene	n/a		tggaaaaatacaattacccccgtattacNtgtgtgga gaaatgaaggcatt
22	GENS026ex5_2	a/g	Verified	Predicted gene	n/a		caglaaatatytaggccctatgic
23	GENS026ex6_1	t/g	Verified	Predicted gene	n/a		aatttattttgtcttttaataaagtaNctct- ctgctcatttggattcgtctatctcgta
24	GENS026ex6_2	t/c	Verified	Predicted gene	n/a		ttatttattgtcttttaataaagta- ctctNctgctcatttggattcgtctatctcgta
25	GENS027ex2_1	a/g	Verified	Predicted gene	n/a		gcaatgcgttttttcttttagtatacaaaNtgaatcctt ctttccctcaaaagctga
26	GENS027pro_1	a/c	Verified	Predicted gene	n/a		ccccaccatctctcgttggcggaagggaNaatg gtatctttaataccaaaaagataat



GenBank accession numbers are provided for the sequences used in this study. The sequences were obtained from GenBank and are available under the accession numbers listed in the table.

27	GENS027pro_2	t/c		Verified	Predicted gene	n/a	alctttgaggctttatgaaccacacatatggtNgaaaa cattgttgccctctggcacaga
28	GENS02ex2_1	a/g		Verified	Predicted gene	n/a	ccatctatgtaggtaacNgaggcaaaagcaaggg ctagggaga
29	GENS02ex3_1	g/c		Verified	Predicted gene	n/a	gggaggcagacattaggcacaataatNacatggat ctctgaaaaacatagctctctacga
30	GENS02ex4_1	t/g		Verified	Predicted gene	n/a	agaggaaatgggtggagtggcagNggggctgggt tctcggctctccccga
31	GENS030ex2_1	a/g		Verified	Predicted gene	n/a	ctggctaggccaaagaactggccaNgltacagtt cccacagagtaccgg
32	GENS030ex3_1	a/t		Verified	Predicted gene	n/a	agggtagtgagggtgtactagggaNctggacact gagccctgaagtgggg
33	GENS030ex4_1	a/g		Verified	Predicted gene	n/a	gcggctgcagggggaggcacaagcNtggggcca ggcgccaagcggc
34	GENS030pro_1	t/c		Verified	Predicted gene	n/a	atgtgtaccatggccaaactaatgttga
35	GENS031ex1_1	t/c		Verified	Predicted gene	n/a	ctgggtaaaaacaggcgcctggacaaaagcNgg aaacagaatgaggctccaggcgttgatt
36	GENS031pro_1	a/t		Verified	Predicted gene	n/a	ccacattttctaatccagctctatcattgNtggacattt gggtgtgtccaaagtcttgc
37	GENS036ex1_1	t/g		Verified	Predicted gene	n/a	tccttcacaggacaggaaatcgcacaaaNaaacat ttcattagcttgcatgtgtaagcat
38	GENS036ex1_2	t/c		Verified	Predicted gene	n/a	aaatggttactgtataccattaccctatctgctttNggg gtgggtggcgcggggggga
39	GENS037ex1_1	a/g		Verified	Predicted gene	n/a	aatagggtcgtgattgagtgacaatgtgagNcaat tagttatcaggagagaagcctaagcgtg
40	GENS037pro_1	a/c		Verified	Predicted gene	n/a	tgaactttagctctcttggtaaataggaaatNgctc caactactgtccacccaagaaac
41	GENS038ex3_1	a/c		Verified	Predicted gene	n/a	tatcgcgcgcctccctccacagctgtcagNcttc atctaattggaaaaagccagatgctcg
42	GENS038pro_1	t/c		Verified	Predicted gene	n/a	tcccctccctgttctgcccgcgtctctgcttNcatctt atctatggggaggagattctccaacct
43	GENS039ex4_1	a/g		Verified	Predicted gene	n/a	ctcttgcataacataatttaataataacNaggaaa aacaataaataactcgtgtggctga
44	GENS039ex7_1	a/g		Verified	Predicted gene	n/a	atgtgccttttctgctctctccctcNtttctctagaagt cctccagaaacc

45	GENS039ex7_2	t/g		Verified	Predicted gene	n/a	ctggagtgccgctacttggccggtgtgacccNctac ggcctgttcttaactctgta
46	GENS03ex2_1	a/g		Verified	Predicted gene	n/a	ataatgcagaacaaattagagaaaaactccNgtc aggctctccactaccatggctgtggct
47	GENS03ex6_1	a/g		Verified	Predicted gene	n/a	aaacaaacaatgccggcagagtcaccNgggct ggccattgaaaagagtacatcag
48	GENS03ex6_2	a/t		Verified	Predicted gene	n/a	gggaggctcttggaacccagagagaccNgtag gagggactgccggcaggagctgtg
49	GENS043ex1_1	a/g		Verified	Predicted gene	n/a	gcggcatctccatcttccaatgaactgagcNtga gcaatgaactgagtgatcagtcctcat
50	GENS043ex2_1	a/c		Verified	Predicted gene	n/a	tactttatctcaatcgcagttggtgaaaaaNtctg caaatagctagccctccagttcaa
51	GENS044ex1_1	t/c		Verified	Predicted gene	n/a	cagtagtctaggaagaagagatgtgattactgcNt ctgtcaatgataaagcagtaagtatcog
52	GENS044ex2_1	t/c		Verified	Predicted gene	n/a	tgtagtaaaacatcaaaaatcctctctcNagctat caagttaattgttaattg
53	GENS044ex2_2	t/g		Verified	Predicted gene	n/a	ctaaactggggctatttctctcatcagccNcattct gctaagccagatgccctgggaag
54	GENS044ex2_3	a/c		Verified	Predicted gene	n/a	tctgctaagccagatgccctgggaagNtctcact gccatctggaaggatgcaga
55	GENS044ex2_4	t/c		Verified	Predicted gene	n/a	ccctgggaagatctcactgcacatcNtgggaaggatg cagaatgtgtgat
56	GENS044ex3_1	a/g		Verified	Predicted gene	n/a	cigtcccatcttccctatacatgtctgaNcccttga gccataacatggatggacagc
57	GENS045ex10_1	g/c		Verified	Predicted gene	n/a	aagctacacaagatgggcatttggcccttiNaccaa catgctgttcttgact
58	GENS045ex10_2	t/c		Verified	Predicted gene	n/a	cagcaaaaccccatgcaaacattcagcatttcaNg gctgaggccacacacagaagccatcag
59	GENS045ex10_3	a/g		Verified	Predicted gene	n/a	aaaccccatgcaaacattcagcatttcaNgtga ggccacacacagaagcc
60	GENS045ex10_4	g/c		Verified	Predicted gene	n/a	ggtagcccaacagatgttctgtgtggtaccaacNga gaaagccatctttaaacagc
61	GENS045ex10_5	t/c		Verified	Predicted gene	n/a	gccatctttaaacagcagagaatctcactgtcNc ctgtccactctctccctgtcaatccccaggac
62	GENS07ex1_1	t/c		Verified	Predicted gene	n/a	ccatctgagacctcatcagccacgaccttacttcca Nataccatcagcattctgttacaac

63	GENS09ex5_1	t/g		Verified	Predicted gene	n/a	ggggcttgcgcagcactgggccNgggacgcaga cccaa
64	GENS09ex5_2	a/g		Verified	Predicted gene	n/a	cagcactggggccggggacgcagaccacaaNacg acagcaggcagcgccgagcg
65	GENS09pro_1	t/c		Verified	Predicted gene	n/a	tgaaggggcccgcacatggcaatgaatcta
66	IGR1000a_1	a/g		Verified	genomic	513	ccaggttggttttNgaactcctggctt
67	IGR1002a_1	g/c		Verified	genomic	418	actctggggccgNgtgtggtggt
68	IGR1002a_2	t/c		Verified	genomic	422	gctgggcccgggtgNgtgggtcacccc
69	IGR1002a_3	g/c		Not yet verified	genomic	477	aggcagggtgatcacNaggtcaagga
70	IGR1002a_4	other/w +	Poly t	Verified	genomic	259	gtaaaatttaNttttttt
71	IGR1002a_5	a/t		Verified	genomic	405	ftagaaaaacNactgctgggccg
72	IGR1003b_1	a/c		Verified	genomic	210	ctcagaaaaacaaaaaNaacaaaaagaac
73	IGR1003b_2	other/w +	Poly t	Verified	genomic	1	taaaaatttaaNttttttttt
74	IGR1004a_2	other/w +	Poly a	Verified	genomic	395	aaaaaNaacaacacttagag
75	IGR1006a_1	t/g		Verified	genomic	389	aactcctgacctaaNgtatccgcctgtt
76	IGR1006a_2	ins/del		Verified	genomic	169	gtttttttNtttgagacagaa
77	IGR1007a_1	t/c		Verified	genomic	190	tttccttaccatNctgtccctcat
78	IGR1007a_2	t/c		Verified	genomic	196	ccatcctgtcNcatatatacaaaact
79	IGR1008a_1	other/w +	Poly t	Verified	genomic	605	tgttgctctctacNttttttt
80	IGR1008a_2	t/c		Verified	genomic	385	tattttgacctcNgtggattctct
81	IGR1009a_1	t/c		Verified	genomic	373	gtgctgggattaNagggtgaaccac
82	IGR1009a_2	t/c		Verified	genomic	389	agggtgaaccactgNtcccagccacttc
83	IGR1010a_1	other/w +	ca repeat	Verified	genomic	186	ttcattatgcacatNacacacac
84	IGR1011a_1	g/c		Verified	genomic	207	ttccatccactgNacagtgtattt
85	IGR1012a_1	t/g		Verified	genomic	520	ggaattctgcaaaaNaacatttcatta
86	IGR1012a_2	t/c		Verified	genomic	556	ggtaagcattgtcNtgcctgcctgt
87	IGR1013a_1	t/c		Verified	genomic	247	accattacctatctgttNgggggtgggtggcgcg
88	IGR1015a_1	a/c	a in ref. sequence	Verified	genomic	202	tcctctcttgagtgctctcaNcggcttctgggtac

89	IGR1016a_1	a/g		Verified	genomic	300	cacgccaccatcNtctagcctggtt
90	IGR1016a_2	ins/del		Verified	genomic	420	atctgctcNtgccttcccc
91	IGR1016a_3	t/g		Verified	genomic	103	ccctacaaccNtctgtcag
92	IGR1017a_1	t/c		Verified	genomic	537	aaggggtcgtcagctccNaaggagtgtagaa
93	IGR1019a_1	t/c		Verified	genomic	366	gagcagcacatggNccaagtggagagctaag
94	IGR1020a_1	t/c		Verified	genomic	590	tccaccagccagaggaactaNtctgttaatt
95	IGR1021a_1	t/g		Verified	genomic	237	gggtatttagagaacaNgggaltgagagctgc
96	IGR1021a_2	g/c		Verified	genomic	314	gcagattttgNtctgtaaat
97	IGR1021a_3	t/c		Verified	genomic	411	agttcataatttaaNgtttttcagg
98	IGR1021a_4	ins/del	2 bp deletion	Verified	genomic	187	ctctttactctNtacctataccat
99	IGR1022a_1	g/c		Verified	genomic	402	aaccctctaaagataattttNaaaggactttctaaag gaa
100	IGR1022a_2	g/c		Verified	genomic	522	gtcaaggccctaactgttttaNtgcctctggtatcgca
101	IGR1022a_3	t/c		Verified	genomic	608	tctagctctggctgNtgagtgctgctgccag
102	IGR1023a_1	a/c		Verified	genomic	477	tttgtaaataggaatatNgtctcaactactgtc
103	IGR1025a_1	other/w +	ca repeat	Verified	genomic	557	ggagattttataNacacaca
104	IGR1026a_2	other/w +	Poly a	Verified	genomic	429	ccctatctcaNaaaaa
105	IGR1026a_3	ins/del		Verified	genomic	520	atgaaatgagatagtcacagctaaaaNgcccgaag ag
106	IGR1027a_1	a/g		Verified	genomic	480	agagcaagctNaggagctc
107	IGR1027a_2	g/c	g on ref. sequence	Verified	genomic	497	gctctggacggcNagccccggaacc
108	IGR1029a_1	a/g		Verified	genomic	497	acaatgtgagNcaatagttt
109	IGR1030a_1	a/g		Verified	genomic	554	agcaciggggNacaatgtt
110	IGR1031a_1	other/w +	Poly t	Verified	genomic	200	tcaggaatgacNttttttt
111	IGR1031a_3	a/c		Not yet verified	genomic	565	aagagctacNgtctaccaa
112	IGR1032a_1	t/c		Verified	genomic	175	ccctaccccNagcagtgaa
113	IGR1032a_2	other/w +	Poly t	Verified	genomic	352	taatgaatttcNttttt
114	IGR1034a_1	a/g		Verified	genomic	293	tgcaatggcNcagctcagct
115	IGR1039a_1	t/g		Verified	genomic	462	ccttggggcacNctactcagcct

116	IGR1040a_1	t/c		Verified	genomic	188	ctggccagaNgggcccctcccc
117	IGR1040a_2	t/g		Verified	genomic	356	aggattccaNgcaggaaagt
118	IGR1040a_3	a/c		Verified	genomic	633	agctgtcagNcttcacttaatt
119	IGR1043a_1	a/g	g in ref. sequence	Verified	genomic	170	ggatctgcacNggaaggaatt
120	IGR1043a_2	a/g		Verified	genomic	377	glactttgttNatttaataat
121	IGR1045a_2	t/c		Verified	genomic	200	ttgacaaaaNtggccatga
122	IGR1045a_3	a/t		Verified	genomic	291	tagaagatttNaaaaattgtaa
123	IGR1045a_4	t/c		Verified	genomic	99	cacagctcaNatccaagccaccccaa
124	IGR1046a_1	t/g		Verified	genomic	301	gtgcatggNtgtcccctcccc
125	IGR1046a_2	t/c		Verified	genomic	337	ttctgttcNcatcttattc
126	IGR1046a_3	t/c		Verified	genomic	572	ttcalactNgttgaatg
127	IGR1047a_1	ins/del		Verified	genomic	253	agagcacaNacacatgga
128	IGR1050a_1	a/g		Verified	genomic	235	ctagatgaagggcataNgcagaagacattt
129	IGR1050a_2	a/t		Verified	genomic	558	gggctgggttcccgNggtgccaagggg
130	IGR1052a_1	t/c		Verified	genomic	319	cctccgtaaatatcttNcagccttfaaacct
131	IGR1055a_1	a/g		Verified	genomic	566	atttaatacNaggaaaaacaat
132	IGR1056a_2	t/g	this base is missing on ref. seq.	Verified	genomic	235	tattaccagggactctctggNgtccactgctttag
133	IGR1056a_3	t/c		Verified	genomic	285	aacccttggctccaagtcNagcagccacagtctt
134	IGR1057a_1	t/c	this base is missing on ref. seq.	Verified	genomic	271	ttcgaagtttcagtgaacNgtccctcgcgaaa
135	IGR1057a_2	a/g		Verified	genomic	390	gacaaagaggtcagcacNtgagtagaacgc
136	IGR1060a_1	g/c		Verified	genomic	279	aaggagcggactctactactaaNgaatcctcctgtaag
137	IGR1060a_2	t/g		Verified	genomic	306	tgtaaagggcgggcccctatNatggtgctggggagaat
138	IGR1063a_2	a/g		Verified	genomic	425	tcctgtcttccctcNtttctctagaagtcctcc
139	IGR1064a_1	t/g		Verified	genomic	335	tggccgtgtgaccccNctacggggcctgtttccta
140	IGR1066b_1	a/g		Verified	genomic	90	taccaaagggccgcctccNggcacttggcgcatgt
141	IGR1068a_1	other/w +	poly T	Verified	genomic	141	ttcttaggtgttgNttttttttttt
142	IGR1070a_2	t/c		Verified	genomic	614	ttccattgttttcaNttggaatttatattttaatgt
143	IGR1070a_2	t/c		Verified	genomic	614	ttccattgttttcaNttggaatttatattttaatgt

144	IGR1070a_3	t/g		Verified	genomic	308	tctaactgtNtctaaactg
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146	IGR1072a_1	t/c		Verified	genomic	337	ctgacatatatttatttaNttatttagtattttttga
147	IGR1092a_1	a/c		Verified	genomic	241	aagcagagccaNacatacatctcac
148	IGR1095a_1	a/g		Verified	genomic	148	agaaagggacNtctggagccagg
149	IGR1095a_2	g/c		Verified	genomic	213	ttttctcgcacNcatagtccttatgca
150	IGR1098a_1	a/c		Verified	genomic	237	gcaagccagaNgacagggccacag
151	IGR1098a_2	g/c		Verified	genomic	294	ccgtcttgaaNcaaaactgctgc
152	IGR1099a_1	other/w +	Poly t	Verified	genomic	216	atgcatggcaltgttcNttt
153	IGR1099b_2	a/g		Not yet verified	genomic	406	tagagacNgagtticacc
154	IGR1099b_3	a/g		Not yet verified	genomic	270	ctggagtNcaatggcacg
155	IGR1100a_1	ins/del	deletion of 1 g t on ref.	Verified	genomic	602	atgaaaactcaacggNtctcagctctgttcta
156	IGR1100a_2	a/t	sequence	Verified	genomic	103	tgatttagaattttattNaaaaaaagicaa
157	IGR1102a_1	t/c		Verified	genomic	605	ttttcttatNgcatttggct
158	IGR1102a_2	t/c		Verified	genomic	400	aattagccaggNggtggagcgcgca
159	IGR1102a_4	a/g		Not yet verified	genomic	119	ctgacattaccagNggaaaaacaatggctg
160	IGR1102a_6	other/w +	Poly a	Verified	genomic	549	cgagactccatctggNaaa
161	IGR1103a_1	other/w +	Poly a	Verified	genomic	78	aaaNgagtttctctg
162	IGR1104a_1	g/c	g on ref. sequence	Verified	genomic	526	cagcttctatgttgNttttattcctcag
163	IGR1105a_1	a/g	g in ref. sequence	Verified	genomic	383	ttaggttcttgggaagcNggtttatgaactaat
164	IGR1107a_1	a/c	a in ref. sequence	Verified	genomic	402	aagattcaatgNaatcagtgactgt
165	IGR1109a_1	a/g	a in ref. sequence	Verified	genomic	415	ggtagatgtgNtattacaagatg
166	IGR1110a_2	ins/del		Verified	genomic	195	aaaaaaNttattaccgg

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167	IGR1111a_1	other/w +	Poly a	Verified	genomic	481		gagctagactctgtctcNaaa
168	IGR1111a_2	a/g	g in ref. sequence	Verified	genomic	318		tctactaaaNatacaaaaa
169	IGR1111a_3	a/g	g in ref. sequence	Verified	genomic	325		atacaaNaattagcc
170	IGR1112a_1	t/c	c on ref. sequence	Verified	genomic	183		aaatacaaatagaNaacatacaaaa
171	IGR1113b_2	a/c		Not yet verified	genomic	293		tacctgaNgtgtgtctg
172	IGR1114a_1	t/c	c on ref. sequence	Verified	genomic	254		gtggctcacacNtgcattcccagcac
173	IGR1114a_2	a/g	a in ref. sequence	Verified	genomic	312		cccaggaagtcNaggctgcagtg
174	IGR1115a_1	other/w +	Poly a	Verified	genomic	465		gagccagactctgtcttNaaaaa
175	IGR1115a_2	a/c		Verified	genomic	307		ctctatctactataaNatacaaaaattag
176	IGR1115a_3	t/c		Verified	genomic	322		atacaaaaattagcNgggtgtgggtggg
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178	IGR1116a_1	t/c		Verified	genomic	625		gactctaagggtgagcNctgaataaagccct
179	IGR1118a_1	a/g		Verified	genomic	192		gtatatgtattagtatNgggtataatcattccaaatg
180	IGR1118a_2	other/w +	Poly a	Verified	genomic	47		ggcaaaaaagagcgaaactctgtcacaataaaN
181	IGR1118a_3	t/c		Verified	genomic	619		agccigccttgttctctaaNaagcctaaattgctag
182	IGR1119a_1	a/g		Verified	genomic	190		aa
183	IGR1120a_1	ins/del		Verified	genomic	258		ccaagctccctcatagNtctcattctgctcag
184	IGR1126a_1	other/w +	Poly a	Verified	genomic	196		tttttcttttttNctgagacagttttttc
185	IGR1142a_1	ins/del	deletion of 2 bp	Verified	genomic	526		agagactccgtctcNaaaaa
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188	IGR1144a_2	a/g		Verified	genomic	611		caicaacaagggttcttaNagaattctctaagg
189	IGR1145a_1	a/g		Verified	genomic	338		aaatgagaaaatctaNaatgaatctcigt
				Verified	genomic			tatcacttctcagtNataaagtctctaa

190	IGR1145a_2	g/c other/w +		Verified	genomic	463	aacaggatattaatctctcacattNcaglaataaa gac
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192	IGR1157b_1	t/c		Not yet verified	genomic	301	aagtctggNatatacac
193	IGR1161a_1	t/c		Verified	genomic	221	cagtctatatcttaaaNgagcaaacagaca
194	IGR1161a_2	t/c		Verified	genomic	662	aaactattttactaaaNagaagtcgccatta
195	IGR1169a_1	other/w +	Poly a	Verified	genomic	384	aaactctatctNaaaaaataaa
196	IGR1169a_2	a/c		Verified	genomic	454	tggtgtgcaNaglaagagaa
197	IGR1172a_1	t/c		Not yet verified	genomic	587	cclaacattaNttcaaaataa
198	IGR1173a_1	a/t		Not yet verified	genomic	517	agtttttNaaattttt
199	IGR1185a_1	t/c		Verified	genomic	516	aaaaattaNaaaaattagc
200	IGR1185a_2	t/c		Verified	genomic	576	aggctgaggNatgggaatc
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202	IGR1186a_2	ins/del		Verified	genomic	423	ttttttNagctctgattc
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205	IGR1196a_2	a/g		Not yet verified	genomic	202	gaagggtcaNacaggaaag
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207	IGR1199a_1	a/g		Verified	genomic	201	atatattccNagaaatgcat
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209	IGR1200a_1	other/w +	Poly a	Verified	genomic	516	gacgaccttttNaaaaaaaaa
210	IGR1218a_1	t/c		Verified	genomic	469	ttttaataacNgtaaaaatgcc
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224	IGR1356a_1	ins/w+		Verified	genomic	172	tagggaggNcattccag
225	IGR1362a_1	t/c	G in ref sequence	Verified	genomic	434	caaggggaagNgcattccag
226	IGR1363a_1	a/g		Verified	genomic	382	gcagtgggNcaaagtgg
227	IGR1364a_1	del/w+		Verified	genomic	147	gtttgttNgtttttgag
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229	IGR1365a_2	ins/w+		Verified	genomic	211	gacittttNaatagagat
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240	IGR1372a_2	t/c		Verified	genomic	323	tctgtgctcNggctggagt
241	IGR1373a_1	t/c		Verified	genomic	338	aactagaaNtctccagg
242	IGR1375a_1	t/c		Verified	genomic	96	aggaattgaaNTtaataga
243	IGR1376a_1	a/t	A in ref sequence	Verified	genomic	462	cacttgtnlgattaat
244	IGR1376a_2	del/w+		Verified	genomic	79	gcaagaagcNcaacaacc

245	IGR1380a_1	other/w	poly t	Verified	genomic	573	agtcaccaacNttttt
246	IGR1380a_2	+		Verified	genomic	155	ttaatatgatNaaatgctcaa
247	IGR2001b_1	a/g		Verified	genomic	148	ccccacaaagNccgagaagcct
248	IGR2002a_1	a/c		Verified	genomic	357	aaaatcgagatgaaggNtttgagcatttcagaga
249	IGR2003a_1	a/g		Verified	genomic	234	tgcagtgagccNagatcacgtcact
250	IGR2004a_1	ins/del	deletion of 14 bp	Verified	genomic	576	tagagttgttcccNagagtttgttccca
251	IGR2006a_1	t/c		Verified	genomic	122	cttagtttcatttNcctactgcca
252	IGR2006a_2	a/g		Verified	genomic	380	ctggctccNaattaataag
253	IGR2007a_1	other/w	Poly a	Verified	genomic	459	taaagtaagaatccctaaggttNaaaaa
254	IGR2008a_1	+		Verified	genomic	646	aag
255	IGR2008a_2	t/c		Verified	genomic	596	ttaacttcgaggagctNtagggagatgaaggaag
256	IGR2009a_1	g/c		Verified	genomic	270	ccctggaggagagctgNggtagaggaaatgac
257	IGR2010a_2	ins/del	deletion of "c"	Verified	genomic	359	ac
258	IGR2010a_3	t/c		Verified	genomic	233	agagtaagtaggggNccttaccaggagcat
259	IGR2010a_4	a/g		Verified	genomic	113	aggctttcgcctNcttcaactcccca
260	IGR2010a_6	a/g		Verified	genomic	329	ggtagggctactNttatltttatggtt
261	IGR2011a_2	a/g		Verified	genomic	43	cctgtcactattaNaccctgcaacggcg
262	IGR2011a_3	a/g		Verified	genomic	153	agcacacggggcaNggtaggcttctgccc
263	IGR2011b_1	g/c		Verified	genomic	396	ggggatcacctcNcctgcgttcggg
264	IGR2011b_2	t/c		Verified	genomic	500	acaggctggggccNggggcgctgggc
265	IGR2013a_1	g/c		Verified	genomic	431	agacgtgcgcccagccccgcgaaNcgagggc
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269	IGR2017a_1	t/c		Verified	genomic	412	aaaggattgaattttgagNgaaaagtt
270	IGR2018a_1	t/c		Verified	genomic	245	ctcgagtagtcctgtgggNtagatcttactaatgic
271	IGR2020a_1	a/c		Verified	genomic	568	ggaagaagtcttacttccNgtgggtgctta
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					genomic		ggccccagctccccNgagacaacatgcagaatt
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					genomic		ac

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272	IGR2020a_15	t/g		Verified	genomic	408	ttccccgactNgcacatccagt
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274	IGR2020a_3	t/c		Verified	genomic	362	ctccc
275	IGR2020a_4	a/g		Verified	genomic	301	acctgtgcttctgtNccccagcactgtcgcc
276	IGR2020a_5	a/g		Verified	genomic	210	gcagggttggtcggNggggtcgtgatgtctgcaa
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280	IGR2021a_3	t/g		Verified	genomic	197	actccaggtgagctgNtccaggtctggc
281	IGR2021a_4	other/w +	gt repeat	Verified	genomic	394	ggccaggggtgcatfttgNgtgtgtgtctctctcct
282	IGR2021a_5	ins/del	deletion of 16 bp	Verified	genomic	277	c
283	IGR2022a_1	t/c		Verified	genomic	612	ccatagggggaggcaagcgacNgggacactag
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287	IGR2024a_1	t/g		Verified	genomic	163	gtgtgNcagagagacagagagacagagagaga
288	IGR2024a_2	a/g		Verified	genomic	461	g
289	IGR2024a_3	t/g		Verified	genomic	517	gcccagcatctgagggNtaggggtgtaatacggc
290	IGR2024a_7	a/g		Verified	genomic	468	a
291	IGR2025a_1	t/c		Verified	genomic	139	aggtcaggagttNgagaccagccctgactaacaatg
292	IGR2025a_2	a/g		Verified	genomic	141	gtgaaa
293	IGR2025a_5	a/g		Verified	genomic	270	aatcagccttagatcNgftaatatgatgtggcttt
							ctgtgtcacctggctgNtgcattgtgccacaagtgc
							c
							ggaaagccaccatNggaaagggaaggcagg
							gccaaagggtgtgatactggctNagaggagctggc
							tca
							atggagaaaagcttggggggcaggNccaggggagc
							agg
							cacattgtgaattagctacNgtgccatgcccttaag
							g
							gggcaggggccaggNgcaggggcgtaaaa
							cctgatgccaccgctcccNtaccctcatacaac
							ctgatgccaccgctcccNccctcatacaacctctt
							ttgccctccatccaNgccattccctgt

294	IGR2025a_6	a/g		Verified	genomic	377	aagctggactctgtNggccocctcaac
295	IGR2026a_1	ins/del	deletion of "c"	Verified	genomic	244	cacaaagaactaccccNttttcagctgagccc
296	IGR2026a_2	a/g		Verified	genomic	314	gtgggtcctctggggcNatgctccctcagccctc
297	IGR2026a_3	ins/del	ins/del "a"	Verified	genomic	611	tcatgtgaacacataNgacgtgtgtaaaatgtga
298	IGR2027a_1	ins/del	ins/del "g"	Verified	genomic	166	aaagtaaatgtttataaNgggtgtggccttttttagag
299	IGR2027a_2	a/g		Verified	genomic	291	a
300	IGR2027a_3	a/c		Verified	genomic	309	gaacagggaacatgcacatNttataaaatcctttcg
301	IGR2027a_4	t/c		Verified	genomic	386	ttataaatcctttcggNcaggcgcggtgggtcacaca
302	IGR2027a_5	other/w		Verified	genomic	386	cctg
303	IGR2029a_1	a/g	Poly a	Verified	genomic	562	tcacctgaggtcaggagttNgagaccagccctgggtg
304	IGR2029a_2	t/c		Verified	genomic	166	aaa
305	IGR2029a_3	other/w		Verified	genomic	562	actccagcccgggcaccNaaaaa
306	IGR2030a_1	t/g		Verified	genomic	112	tgaaccgggagatgNaggttcagtgagct
307	IGR2031a_1	t/g		Verified	genomic	415	tcagccctgggtgacaagagNgagactttgtctca
308	IGR2031a_3	t/g		Verified	genomic	180	aa
309	IGR2031a_4	a/g		Verified	genomic	180	ttgtctcaaaaaaaaaaaatccttttg
310	IGR2031a_5	t/g		Verified	genomic	539	gaaggtgtggatatgtgcNtttcctgtctccct
311	IGR2032a_1	ins/del		Verified	genomic	415	gatgctgtgtgagtgggcaggNggactcctgctggg
312	IGR2032a_2	a/g		Verified	genomic	40	ta
313	IGR2032a_3	other/w		Verified	genomic	227	tggtgatatgtgcNtttcctgtctccct
314	IGR2033a_1	t/c		Verified	genomic	227	cicagtcgccagaaaccNtatgtactgtgac
315	IGR2034a_1	t/g		Verified	genomic	232	cicagtcgccagaaaccataatgNactgtgaccccgcc
316	IGR2036a_1	g/c		Verified	genomic	126	tcact
317	IGR2036a_2	a/g		Verified	genomic	356	tcctactaaaaaNaactaaccaggcggtgggtgg
318	IGR2037a_1	ins/del	ct repeat	Verified	genomic	278	ggaacagaggNatagacagga
319	IGR2038a_1	ins/del	aaac repeat	Verified	genomic	587	agactctgtctcNaaaaa
320	IGR2039a_1	ins/del		Verified	genomic	441	atcattctaaggaNctgacagtgcttctg
321	IGR2041a_1	a/g		Verified	genomic	356	gaagctaataNgcaaacatc
322	IGR2041a_2	a/g		Verified	genomic	183	acctcaaaagtNtggctggata
323	IGR2041a_3	ins/del		Verified	genomic	534	glaagacacaNgcctgcagag
324	IGR2041a_4	ins/del		Verified	genomic	532	aagacaacctagtctNctgttctgtcttaaa
325	IGR2041a_5	ins/del		Verified	genomic	394	tgagttctacacagtggtNaacaaca
326	IGR2041a_6	ins/del		Verified	genomic	331	tgcttggctNgttggat
327	IGR2041a_7	a/g		Verified	genomic	331	cacgtattaagccaccctacNatataccacc

322	IGR2042a_2	t/c		Verified	genomic	270		gagggccaaaggcttgcctgcccNctcctgccct
323	IGR2043a_1	a/g		Not yet verified	genomic	334		tctgtagtggtgcNggaacatcctgact
324	IGR2047a_1	other/w +	Poly t	Verified	genomic	225		tgaggggctttgcNttttt
325	IGR2049a_2	t/c	t on ref. sequence	Verified	genomic	332		gaccctgctacatNgtacataacaatagctata
326	IGR2051a_1	t/c	t on ref. sequence	Verified	genomic	470		ggcagggNtgtctgggcaaggaccagtc
327	IGR2051a_2	a/g		Verified	genomic	605		acacttattNtaactgtcacccctgggccat
328	IGR2052a_1	t/c		Verified	genomic	290		gctattttctcNtgttatttcagtgaccagg
329	IGR2052a_2	a/g		Verified	genomic	106		ttgacaaacactattNtaactgtcacc
330	IGR2053a_1	a/g		Verified	genomic	225		cattcactgtgtcttNgggctagagaaga
331	IGR2053a_2	a/c		Verified	genomic	369		cactgtgtctgtcagtgacNcctgttccccctaa gt
332	IGR2053a_3	t/c		Verified	genomic	544		gtgaccctattggatcttctcaNgccactgaggat at
333	IGR2054a_1	t/c		Verified	genomic	196		caagagggaatggagcttNgcagaggggctg
334	IGR2054a_2	ins/del	ins/del 6 bp	Verified	genomic	591		cttctgtctgtctgtNccctctgctc
335	IGR2055a_1	t/g		Verified	genomic	609		gagtggttttgagaagaNtctgaggagtgaggac
336	IGR2056a_1	a/g		Verified	genomic	153		tttttaagactagtcNctgggcgcggt
337	IGR2056a_2	a/c		Verified	genomic	364		gagaaTggcgtgaacccgggaggNagagcttgc agt
338	IGR2056a_3	other/w +	Poly a	Verified	genomic	481		aagcgagactccatctcNaaaaaaacaaaa aaciaa
339	IGR2056a_4	g/c		Verified	genomic	432		gagctgcagtgagctgaNatcgccactgcact
340	IGR2057a_1	a/g		Verified	genomic	421		gaagTgaaaaccaaataNcaaggggtacaga
341	IGR2060a_1	g/c		Verified	genomic	514		ttgcaaccttNgcaaaaggtaa
342	IGR2061a_3	t/c		Verified	genomic	236		catacacagaagaaNgagttccatttactg
343	IGR2062a_1	ins/del	caaa repeat c on ref. sequence	Verified	genomic	195		aaaaacaaacaaacaaacaaacaaNacacigt catgcc
344	IGR2063b_1	g/c		Verified	genomic	218		ggcaaaataatNacatggatctc
345	IGR2063b_2	t/g	t on ref. sequence	Verified	genomic	369		agttggcagNggggctgtgtc

346	GR2064a_1	a/c		Verified	genomic	364	aaactgtgatttNcagtttcattt
347	GR2064a_2	a/g		Verified	genomic	508	ccctcagagggcNggtactggact
348	GR2066a_1	t/c		Verified	genomic	459	cttatctctccctcgccaanGgaagctggttggtgccccc
349	GR2067a_1	a/g		Verified	genomic	163	agccactactftgggcNgctcagctc
350	GR2067a_2	a/g		Verified	genomic	243	cacacttccccacNagaataaagcaagca
351	GR2067a_3	t/c		Verified	genomic	266	agcaagcagctgttNctctcttggggccc
352	GR2067a_4	a/g		Verified	genomic	485	agcctgagcctNgcgcacgcccagac
353	GR2068a_1	other/w +	ca repeat	Verified	genomic	354	acacacacacacaNttttttgagagagag
354	GR2068a_2	g/c		Verified	genomic	70	algtgtagtgtgtgagaaNgltgtgagaggtactcg
355	GR2069a_1	a/g	g in ref. sequence	Verified	genomic	394	ttatgttccattgtacNtatccaccatatittt
356	GR2069a_2	t/c		Verified	genomic	425	atccactctctNtgtcatgtgacatctg
357	GR2070a_1	t/c		Verified	genomic	551	tctaagaaaaaagaaagcNgtgaaltcttggac
358	GR2071a_1	t/g	g on ref. sequence	Verified	genomic	165	gctctgtgccaggcaggggNctccgaggtgagtgt
359	GR2071a_2	a/t	a on ref. sequence	Verified	genomic	171	ccaggcagggggctccgNngtgagtgtggcct
360	GR2071a_3	a/g	a in ref. sequence	Verified	genomic	365	agagaaggggaactggcNtgtgtggctgggctgtg
361	GR2072a_1	a/g	a in ref. sequence	Verified	genomic	312	gcaggctcagtgaaggagaggNgctctccttatg
362	GR2072a_2	t/c	t on ref. sequence	Verified	genomic	408	atggggaactctcctaNaactgtcggaggcggtg
363	GR2073a_1	a/c	a in ref. sequence	Verified	genomic	94	agtcatggcactaNatggagcccagg
364	GR2073a_2	a/g	a in ref. sequence	Verified	genomic	313	caccaggaggttcagcNcccactgtgg
365	GR2073a_3	t/c	c in ref. sequence	Verified	genomic	379	gcattcccagcgccNggccagtggtcc
366	GR2074a_1	ins/del		Verified	genomic	239	gagtaaggggtcNaggaggggggggttggc
367	GR2076a_1	t/c	t on ref. sequence	Verified	genomic	184	gaacatactcataNccatgcttcccc
368	GR2076a_2	other/w +	Poly t	Verified	genomic	647	taccttatgtgtttgtgcNtttttttt

369	IGR2077a_1	other/w +	Poly t	Verified	genomic	148		taagggttggtgcNttttttttt
370	IGR2078a_1	a/g	g in ref. sequence	Verified	genomic	197		gcagggtggggagaaNgccagactcaggggtg
371	IGR2078a_2	ins/del	ins/del "c"	Verified	genomic	67		ggccagccccccccNggaagtggat
372	IGR2079a_1	ins/del	Poly a	Verified	genomic	345		gtaaaaaaaNccctacagggtaaaaag
373	IGR2079a_2	t/c	t on ref. sequence	Verified	genomic	582		ccccatgtgccaNgtcacctccctgtc
374	IGR2081a_1	a/g	a in ref. sequence	Verified	genomic	140		ccagcaggaaacaNatgcaca
375	IGR2081a_2	a/t	t in ref. sequence	Verified	genomic	315		gaaccagagagaccNgtaggagggg
376	IGR2081a_3	a/g	a in ref. sequence	Verified	genomic	622		gcccggcagagtcaccNgggctggcc
377	IGR2083a_1	t/c		Verified	genomic	372		aaatggggccaggNgcgggtggctca
378	IGR2083a_2	ins/del		Not yet verified	genomic	199		ccgtcttaaaaaaaaNNNgctgggtgtggtg
379	IGR2083a_3	a/g	g in ref. sequence	Verified	genomic	572		aattgctgaacccNggaggcagaggtt
380	IGR2084a_2	ins/del	ccaa repeat	Verified	genomic	166		ccaaccaaccaNccaaatggattaaacttc
381	IGR2085a_1	t/c	c on ref. sequence	Verified	genomic	131		cacttaccttgccNgcgccaccc
382	IGR2085a_2	a/g	a on ref. sequence	Verified	genomic	249		tcctcttgaacctNgtggattct
383	IGR2085a_3	a/g	a on ref. sequence	Verified	genomic	437		tggtcaacagtcaccaNctgagcccagcc
384	IGR2085a_4	a/g		Verified	genomic	368		cttgaggigccicNtaagagggtccaatga
385	IGR2085a_5	t/c		Verified	genomic	538		ttattccagtcacctNgagtcattccagtc
386	IGR2087a_3	other other/w	gaa repeat	Not yet verified	genomic	193		agggaagaagaagaaNcaagaggaagagga
387	IGR2087a_4	+	Poly a	Verified	genomic	504		gaaagccaaaaattaaaaaaaNcaacagaa
388	IGR2090a_1	a/c	a in ref. sequence	Verified	genomic	219		agtcaggctgtctcggcNgctaaaagagggc
389	IGR2090a_2	t/c		Verified	genomic	360		tgttggtggggctcNagcgttaccgccc
390	IGR2090a_3	t/c	c on ref. sequence	Verified	genomic	444		ttcaccattgtctcNctattcccttt

391	IGR2090a_4	other/w +	Poly t	Verified	genomic	532		acttacctgctgaaatgcactgNttttttt
392	IGR2091a_1	t/g	a in ref. sequence	Verified	genomic	581		taatgacattccctctgtatNgaatgtgccaatgtgga
393	IGR2091a_3	a/c		Not yet verified	genomic	391		gatcacattatNttgcctgagtt
394	IGR2091a_4	t/c		Not yet verified	genomic	404		ttgcctgagttcNcaagttggttaagaga
395	IGR2091a_5	ins/del		Not yet verified	genomic	547		tctcatcaataaataatttatNNNcttcatt
396	IGR2092a_2	ins/del	Poly a	Verified	genomic	435		aaaaaaaaaaaaaNgccaggcg
397	IGR2093a_1	ins/del	Poly a	Verified	genomic	229		aaaaaaaaaaNgccctagacctctg
398	IGR2093a_2	a/g	g in ref. sequence	Not yet verified	genomic	123		ttggaggctgaggcNgaagaatcgct
399	IGR2093a_3	t/c		Verified	genomic	181		agattgcccactgNgcttcagct
400	IGR2093a_4	a/g	g in ref. sequence	Verified	genomic	318		gggagacccggaggaggNtagggaagt
401	IGR2095a_1	t/c	c on ref. sequence	Verified	genomic	421		caacagcctggcagNgaggcctgtct
402	IGR2096a_1	a/c	c in ref. sequence	Verified	genomic	112		actagagggtttttaNagagaagtgcacatgat
403	IGR2096a_2	a/g		Verified	genomic	498		taagggaatacggttttgNacgtaagtgtgagatgcc
404	IGR2097a_1	a/c		Not yet verified	genomic	58		caggtggaaNtgtgaatctggggagag
405	IGR2097a_2	ins/del	Poly a	Verified	genomic	463		aagacictgtctcNaaaaa
406	IGR2101a_1	t/c		Not yet verified	genomic	283		ccagaatagagaccacNtccatcctcctt
407	IGR2102a_1	g/c	g on ref. sequence	Verified	genomic	166		gaacttagatttgcgNcccttagcatcacaac
408	IGR2102a_2	t/g	g on ref. sequence	Verified	genomic	223		caatgcatgatcctNctgagccctcagc
409	IGR2105a_1	a/t		Not yet verified	genomic	493		ttgatactcagtaNgtacagcttatt
410	IGR2106a_1	other/w +	ct repeat c on ref. sequence	Verified	genomic	137		caggcaacaaaNtctcctcct
411	IGR2107a_1	t/c		Verified	genomic	300		ccttgtctcaaNtgtctcagctctalc



412	IGR2107a_2	t/c	t on ref. sequence	Verified	genomic	564	ccaaaggtcNcaggctctggc
413	IGR2108a_1	ins/del		Verified	genomic	360	ccattccctgagcNcaggtgcctttct
414	IGR2109a_1	a/g		Verified	genomic	400	ggccaggctggtctcNgctagactcaagtg
415	IGR2110a_1	t/c		Not yet verified	genomic	286	tgttgagacagggctctgNctgtgctccaggatgg
416	IGR2110a_2	other/w +	Poly t	Verified	genomic	420	atgccagctaNttttt
417	IGR2111a_1	a/g		Verified	genomic	55	ccaccgcaccggccaNttttattgttttaaa
418	IGR2111a_3	t/c	c on ref. sequence	Verified	genomic	516	ttgccaacatttggtatNatcagtgcttcaatttt
419	IGR2112a_1	other/w +	Poly t	Verified	genomic	285	tttttttNctgagacagagtgctcgct
420	IGR2114a_1	other/w +		Verified	genomic	3331	caattgacttcctcNaaaaa
421	IGR2117a_1	a/g	Poly a	Verified	genomic	355	aagggtgctctagNgcacacactcctccc
422	IGR2121a_1	other/w +	Poly a	Verified	genomic	609	aataaagtgattacttNaaaaaaaaa
423	IGR2121a_2	a/t		Verified	genomic	117	gaggcctgacagNttgaaggggtg
424	IGR2121a_3	t/c		Verified	genomic	815	cctctgggtNtttccaaatca
425	IGR2123a_1	a/g	g in ref. sequence	Verified	genomic	230	ttgccagaacacNgggtcagagagcaagag
426	IGR2125a_1	other/w +	Poly a	Verified	genomic	546	agagtgagactgtctcaaaaaaaaaa
427	IGR2126a_1	a/g		Verified	genomic	364	cttcatactacttNgaaaaccatat
428	IGR2126a_2	other/w +	Poly a	Verified	genomic	47	gagactgtctcNaaaaa
429	IGR2131a_1	other/w +	Poly a	Verified	genomic	249	aaaaaaaaaNgaacctgtcgta
430	IGR2134a_1	a/g	a on ref. sequence	Verified	genomic	339	acttcagattaataNgtcttaacccat
431	IGR2136a_2	t/c		Verified	genomic	444	tgtctagctccatttgagNagggacctt
432	IGR2138a_1	a/g		Verified	genomic	375	atgatttgcNtcaaaagcag
433	IGR2144a_1	t/g		Not yet verified	genomic	384	tcagtaaccacatctgtNtttcaatgctctt
434	IGR2144a_2	other/w +	Poly a	Verified	genomic	463	acagaggtaaaagtgtttgaagcNaaaaa

435	IGR2144a_3	a/t		Verified	genomic	127	ctagcctaNggtctaggccc
436	IGR2144a_4	t/c		Verified	genomic	137	ggctaggcNctcgtcctg
437	IGR2144a_5	a/g		Verified	genomic	166	ggaatcattacNtatcacaatca
438	IGR2147a_1	a/g		Not yet verified	genomic	354	accatggatgcNtagctgagttcctg
439	IGR2148a_1	t/c		Verified	genomic	253	acagttgtcccNagcatcttcgagga
440	IGR2148a_2	other/w		Not yet verified	genomic	619	gagacttcatcNaaaaacaaaaacaaaaa
441	IGR2150a_1	+	caaaaa repeat	Verified	genomic	90	caaaaa
442	IGR2150a_2	g/c		Verified	genomic	336	aaactctaccacNactgaaatctggtta
443	IGR2150a_3	t/g		Not yet verified	genomic	558	cctggggctctaNtattgggtgttac
444	IGR2151a_1	+		Verified	genomic	202	gaaagatatataNaaattaaattaaa
445	IGR2151a_2	a/g	Poly a	Verified	genomic	566	aaaaNtcataccattagtctcacttaaa
446	IGR2153a_1	a/g	a on ref. sequence	Verified	genomic	423	catctgtcaNccccagcttc
447	IGR2154a_1	a/g		Not yet verified	genomic	389	cagaacaaaattagagaaaaactccNgtcaggctc
448	IGR2155a_1	a/c		Not yet verified	genomic	398	tccac
449	IGR2155a_2	a/g		Not yet verified	genomic	619	acaacaaagggtaNatatttttaggtctc
450	IGR2156a_1	a/c		Not yet verified	genomic	176	attattagtNaataatcacc
451	IGR2157a_1	a/c		Not yet verified	genomic	254	aaggcgggtNcagtggtcac
452	IGR2159a_1	other/w	Poly t	Verified	genomic	411	ctaggcaggltggatcatNtgagggtcagg
453	IGR2160a_1	+	ca repeat	Verified	genomic	601	tggaagagacatgcattNcaaacattatc
454	IGR2160a_2	a/g		Not yet verified	genomic	213	tttttttttNccgtgaacag
455	IGR2160a_3	a/g		Not yet verified	genomic	287	acaggcgcgNcacacacacacacaca
456	IGR2162a_1	a/c		Not yet verified	genomic	350	taaaaattattcgNgagaatttttagaa
				Not yet verified	genomic	287	ccaagtaccttggNctgtactgagagaiga
				Not yet verified	genomic	350	acaacaaaaacaaNcaaaccttatt

457	IGR2162a_3	t/c		Not yet verified	genomic	450		aaatatagNcaaaataact
458	IGR2164a_1	a/t		Not yet verified	genomic	557		tcttgcccaacNtggtaaaccccc
459	IGR2165a_1	ins/del	Poly a	Verified	genomic	473		ggaaaaaaaaaNcacacatgat
460	IGR2165a_2	ins/del		Not yet verified	genomic	271		ataaaaaaaaaaNgatttattatgt
461	IGR2166a_2	a/c		Not yet verified	genomic	323		agtttcNgtttagaaaag
462	IGR2167a_1	t/c	c on ref. sequence	Verified	genomic	324		acttaagagaNlcaaaataatttt
463	IGR2167a_2	a/t		Not yet verified	genomic	207		tttaaaacttNtaaaggaat
464	IGR2168a_1	ins/del		Not yet verified	genomic	341		tgtttctttttctttcttNtttttttagacggag
465	IGR2175a_1	a/g	g in ref. sequence	Verified	genomic	310		tggggccaaaaaatctcNtctgacttccagtg
466	IGR2175a_2	a/g	g in ref. sequence	Verified	genomic	526		tccaagggtcacatNgttactatgtatgtt
467	IGR2176a_1	a/g	g in ref. sequence	Verified	genomic	119		gaagcaagactgtcNggaacactggactc
468	IGR2176a_2	a/g		Not yet verified	genomic	399		aaccatctgtttgtgtcNtgagggtctctgtat
469	IGR2177a_1	a/c	c in ref. sequence	Verified	genomic	325		tgatgatcacgcaacNcagctgaagaatgat
470	IGR2178a_1	a/g		Verified	genomic	138		ccatcctaaatactacaagatgcNtttgacgtata
471	IGR2179a_1	a/g		Verified	genomic	284		aga
		other/w						aaagtcaaaaaatcNaaaggagatgagca
472	IGR2179a_2	+	Poly t	Verified	genomic	371		ttctgggaaaagggaagtcNtttttttttt
473	IGR2179a_3	ins/del		Not yet verified	genomic	470		taatctctgccctccaggNlcaagtgattctct
474	IGR2180a_1	a/g		Not yet verified	genomic	65		gtatttttagtagagacNgggtttccttatgtt
475	IGR2180a_2	g/c		Verified	genomic	383		tcaccagcaacctgttNtgagtgaaatc
476	IGR2181a_1	+	Poly t	Verified	genomic	260		aaaaagttttttttttNctaccaaatgtacag

477	IGR2181a_2	t/c		Verified	genomic	416	attacattataattacaNgcataat
478	IGR2181a_3	a/g		Verified	genomic	614	ccaagaaagaggNgtcatgggtaa
479	IGR2181a_4	a/c		Verified	genomic	83	gtggaggctgaNagtaggcgagttt
480	IGR2182a_1	a/g		Verified	genomic	115	tgccccaagaaagaggNgtcatgggtaaacc
481	IGR2184a_1	other/w +	Poly t	Verified	genomic	58	tccttcattttagcccgaaagactcccttagcaNttttt
482	IGR2184a_4	a/t		Not yet verified	genomic	448	tgccatgtgtgtNgtctgcaccc
483	IGR2184a_5	ins/del	ins/del t	Verified	genomic	380	tattttttttttaagctacNttaagttctagggt
484	IGR2185a_2	t/c		Not yet verified	genomic	420	gttctagatccNtgaggatc
485	IGR2185a_3	t/g		Not yet verified	genomic	453	ttccacaatggtNgaactagttt
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487	IGR2188a_1	t/c		Not yet verified	genomic	549	tttgctgaagttgNttatcaacttaa
488	IGR2189a_1	a/g		Verified	genomic	475	atatgatgcattacNtttatcgatttg
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490	IGR2190a_2	t/c		Not yet verified	genomic	343	ttatggccNcaatttc
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492	IGR2191a_1	a/g		Not yet verified	genomic	286	tggtgattttNgatgttcc
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494	IGR2191a_3	a/g		Not yet verified	genomic	390	ttgtgtctttgttctcNttggtttcaaa
495	IGR2191a_4	a/t		Not yet verified	genomic	498	gcgggttttgaNtgagtttctt
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497	IGR2192a_2	t/c		Verified	genomic	506	ccccgcNttttttg
498	IGR2192a_3	t/g		Verified	genomic	359	ttatgaatctgggNgctccgtatt
499	IGR2193a_1	t/g		Verified	genomic	361	ttcaggagctcttNtaaggcagg

500	IGR2193a_2	t/g	Verified	genomic	376	ggcctggNgtgacaaa
501	IGR2193a_3	t/c	Verified	genomic	423	atttatttcNcctcacttat
502	IGR2194a_1	a/g	Verified	genomic	57	cagagagatccNctgttagtctga
503	IGR2194a_2	a/g	Verified	genomic	196	agagtatctttNgggttctctg
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506	IGR2198a_1	+	verified	genomic	233	cagtagacgaacNatgcaaaaatacca
507	IGR2198a_3	a/t	Not yet	genomic	98	tctggggctttNacgttttttagtg
508	IGR2199a_1	t/c	Verified	genomic	357	cagagataagaaNtagttccaagaa
509	IGR2200a_1	a/c	Verified	genomic	176	acaggcttNgacagaggacttggga
510	IGR2202a_1	t/c	Verified	genomic	308	tcactaaattctagaaaNaaagattctaggcagt
511	IGR2202a_2	a/t	Not yet	genomic	330	taggcagttgtcgtNtatttaaaaaaatcat
512	IGR2202a_3	a/g	Verified	genomic	528	caggactaaagtgaNctactctgaaaga
513	IGR2202a_4	ins/del	Not yet	genomic	622	tttttgacacacacaatgacacNcacttagagaa
514	IGR2203a_1	a/g	Verified	genomic	329	gtgc
515	IGR2203a_2	other/w	Verified	genomic	216	acaaacaaataaacaNtaaaacaaaaccaca
516	IGR2204a_1	+	Verified	genomic	584	cagagtattctgtgtttNaaaaaaaaa
517	IGR2206b_1	ins/del	Not yet	genomic	520	acagcaaaggccctttNactgaaggactc
518	IGR2207a_1	t/g	Not yet	genomic	428	aggggcggttgagNagaagagctgggccc
519	IGR2209a_1	a/c	verified	genomic	153	ggfataataattttNcgttcalcagacctc
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521	IGR2209a_3	g/c	Verified	genomic	462	gcactttccctcaaNctggagaccaccag
522	IGR2210a_1	a/g	Verified	genomic	297	ggccatcagaatctcNagtgtatcttctaa
523	IGR2210a_2	g/c	Verified	genomic	610	tcctgctaaggNcctgtgaggccc
524	IGR2213a_1	t/c	Verified	genomic	314	catctagggtgtaNgttccatgagg
525	IGR2214a_1	g/c	Verified	genomic	318	cggtaactgtggagcaNagagggtggctcccaa
526	IGR2215a_1	a/t	Verified	genomic	198	taaccaccaggctccagaNgtcgcctagaatcc
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		a/g	Verified	genomic		cc

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527	IGR2221a_1			Verified	genomic	261		gaaaaaaggaaaaaNattagcatgttta
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532	IGR2222a_1	a/g	g in ref. sequence	Verified	genomic	476		cagagtccacgcgaNagcaccgccgcat
533	IGR2222a_2	t/c	c on ref. sequence	Verified	genomic	194		tttttggtctctctatttaaNatggtatctttgtga
534	IGR2223a_1	ins/del		Not yet verified	genomic	485		gcctcaaggNaagaatatt
535	IGR2223a_2	other/w +	at repeat	Verified	genomic	300		ctccaaccatgccNccctcttctggggc
536	IGR2224a_1	a/g		Verified	genomic	387		gagtctagtaaatlgacNaccaagtaactaagac
537	IGR2224a_2	t/c		Verified	genomic	389		cctagtaaatlgactaNcaagtactaagaccaa
538	IGR2224a_3	t/c		Verified	genomic	582		tgaggacatcacagNgtctccagaaaaggta
539	IGR2224a_4	t/c		Verified	genomic	464		agtcctggctctcaNagtgccatgtctatt
540	IGR2225a_1	a/c		Verified	genomic	204		taaagagaaaagaaNcattgtctctgatt
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542	IGR2226a_2	t/g	t on ref. sequence	Verified	genomic	524		ggaatgtctgaaNtgcatactcagtgt
543	IGR2226a_3	t/c		Verified	genomic	272		taagaggtagtatcaNgtacaaaagtattct
544	IGR2226a_4	t/c		Verified	genomic	450		gatattcacagtatagtgNggagagaccaacatta
545	IGR2228a_1	g/c	g on ref. sequence	Verified	genomic	298		ttttctgtgtgttNttttttccatcac
546	IGR2229a_1	t/g	t on ref. sequence	Verified	genomic	608		catacttttagccaNtttagggigtatt
547	IGR2230a_1	t/c		Verified	genomic	597		tgtgaaacctgggNaagttatttaa
548	IGR2233a_1	g/c	g on ref. sequence	Verified	genomic	362		taatccagcacaactcNggaggctgagaca
549	IGR2234a_1	a/g		Verified	genomic			

550	IGR2234a_2	g/c	g on ref. sequence	Verified	genomic	395	gaatcttgaccigNgaggcagaggttgca
551	IGR2235a_1	t/c		Verified	genomic	153	gtgttcacatgNcatgtggccaagga
552	IGR2235a_2	t/g		Verified	genomic	386	agttaaaagctttaNaattatacaaat
553	IGR2236a_1	a/g		Verified	genomic	256	ttacctagtcacccgNtcacagatacatca
554	IGR2236a_2	ins/del		Not yet verified	genomic	321	atttgaattacggagtcagatNttggctcttctact
555	IGR2236a_3	t/c		Verified	genomic	441	gaaggccaggcacaNgtcttctcctcagtg
556	IGR2237a_1	a/g		Verified	genomic	395	agcaaggcctctaacNctgtctcctctaaaaatc
557	IGR2237a_3	a/g		Verified	genomic	619	tggccaatgacccccNggctctttttgtgac
558	IGR2238a_1	a/g		Verified	genomic	92	cctgtctgtctcNggttccaccctg
559	IGR2238a_2	a/c		Verified	genomic	115	accctgggccaatgaNccccggggtctttt
560	IGR2238a_3	ins/del		Not yet verified	genomic	247	gctccactctactattNacttctcaacct
561	IGR2238a_4	a/g		Not yet verified	genomic	442	tggatctggctNcgctgcctctaaaca
562	IGR2239a_1	a/c		Not yet verified	genomic	256	ctgttctcgcactgNtgggcagtggtggg
563	IGR2240a_1	t/c		Verified	genomic	545	agtgtcattttgagaNaggccccagagcat
564	IGR2242a_1	t/g		Not yet verified	genomic	119	gtgggttaagattNgggtcacagtgcta
565	IGR2243a_1	a/c	c in ref. sequence	Verified	genomic	256	tgccccctgtatNgaagagagggc
566	IGR2244a_1	other/w +	Poly t	Verified	genomic	220	ttttttttNggctccttgaccc
567	IGR2244a_2	g/c	c on ref. sequence	Not yet verified	genomic	73	ccaccagcctggNtaattttgt
568	IGR2244a_3	t/c	t on ref. sequence	Verified	genomic	469	gaggttcagNtccagggtctct
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570	IGR2245a_2	a/g		Verified	genomic	145	aggacaatgggNaggagtgaggag
571	IGR2245a_3	a/g	g in ref. sequence	Verified	genomic	397	attacaggcaccNccaccacgcaggg
572	IGR2245a_4	t/g		Verified	genomic	434	atttttagcgaNacgaggtttcacca
573	IGR2245a_5	t/c		Verified	genomic	574	tgtctgtccaNaggctggacag
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575	IGR2246a_1	ins/del		Verified	genomic	629	ccaccacgccccctgccaNtatttttta

576	IGR2248a_1	t/g	t on ref. sequence	Verified	genomic	145	ctagatgcagtgNtcagcaggccag
577	IGR2249a_1	a/g	a in ref. sequence	Verified	genomic	289	aactgaanGgtccaatttcct
578	IGR2250a_1	t/c		Verified	genomic	145	ggctcagcaccacaNccagcagggtt
579	IGR2250a_2	t/c	t on ref. sequence	Verified	genomic	253	ttctgtctgtgcaNtggggcctca
580	IGR2250a_3	t/g	t on ref. sequence	Verified	genomic	302	acaccctaggctcacNgagaggcctcc
581	IGR2250a_4	t/c	c on ref. sequence	Verified	genomic	389	tatcaatgagggtatNtcactgggtacttac
582	IGR2251a_1	g/c	c on ref. sequence	Verified	genomic	269	taatccagcttgNaggcagaagcagg
583	IGR2251a_2	a/t		Verified	genomic	360	aaacacaaaaatNgtgggcgtgtgg
584	IGR2251a_3	a/g	g in ref. sequence	Verified	genomic	392	cagctactcggagNctgaggcaggag
585	IGR2251a_4	g/c		Verified	genomic	436	aggcgaagattgcaNtgagccaagaacg
586	IGR2251a_5	+	Poly a	Verified	genomic	526	tgacagaggagagactctctctctNaaaaaa
587	IGR2252a_1	a/g		Verified	genomic	323	cccaactagagtaaNtctggacacacag
588	IGR2252a_2	t/c		Verified	genomic	405	tgccatcaggaNgggaggccagactg
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590	IGR2254a_1	t/g		Verified	genomic	68	agcgcggcctggggtcNgggaacgcgg
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592	IGR2255a_2	a/g		Verified	genomic	217	gaggctgggagctNtgacttttcatt
593	IGR2255a_3	+	Poly a	Verified	genomic	387	tcagaagctaactggNaaaaaaa
594	IGR2256a_1	t/c		Verified	genomic	510	atcatagtcaccgcagNcctgaactcctaagctt
595	IGR2256a_2	+	Poly a	Verified	genomic	344	ttctcaggatttgNaaaaaa
596	IGR2256a_3	a/g		Verified	genomic	179	tgaataaactttaNtggatatattaa
597	IGR2257a_1	a/g	g in ref. sequence	Verified	genomic	423	atataatgtgtgNgtaaagaatat
598	IGR2257a_2	t/c	t on ref. sequence	Verified	genomic	508	cagcagatttttaaNaaggaaatctaa



599	IGR2257a_3	g/c		Verified	genomic	621	ctattctacttcNtgaagatggatgg
600	IGR2258a_1	other/w +	Poly t	Verified	genomic	575	tgcaNttttttt
601	IGR2259a_1	other/w +	Poly t	Verified	genomic	234	gctaNttttttg
602	IGR2260a_1	t/c		Not yet verified	genomic	582	tcaacaataNgttaataataa
603	IGR2261a_1	t/c		Verified	genomic	608	ggctgaggaggNggatcacc
604	IGR2262a_1	ins/del	Poly a	Verified	genomic	332	aagactccgtctcNaaaaaa
605	IGR2262a_3	a/g	a in ref. sequence	Verified	genomic	425	ttcagagcNtctgtccag
606	IGR2263b_1	g/c	g on ref. sequence	Verified	genomic	411	ttcaagtgaltctNctgtctcagcctcc
607	IGR2264a_1	other/w +		Verified	genomic	318	taatagctgttttttNtgccaaaaatcacgtg
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610	IGR2269a_1	a/g		Not yet verified	genomic	270	tatgtacaagtatctNtttgagtactgct
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612	IGR2272a_2	t/c		Verified	genomic	163	ctcttggaaggctgNggcaggaaagatgc
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616	IGR2273a_1	other/w +	Poly t	Verified	genomic	388	cccttatccacagNttttttttt
617	IGR2274a_1	t/g		Verified	genomic	311	tctccatgtcacccgcaNtcacattgtgtgtgg
618	IGR2274a_2	g/c		Verified	genomic	381	tcattagccgtggcttNcattctctctgaac
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620	IGR2276a_1	t/c	c on ref. sequence	Verified	genomic	113	cactactcatctcNtgagcacaaaaag

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623	IGR2277a_2	+	Poly t	Verified	genomic	485	galgcaagaaNtttttttttttt
624	IGR2279a_1	a/g	a in ref. sequence	Verified	genomic	165	acaggcatccaccaccNigccctggtaattt
625	IGR2279a_2	t/c	c on ref. sequence	Verified	genomic	256	catgtatctgccNgccicagccttccaaa
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628	IGR2279a_5	t/c		Verified	genomic	277	gccttccaaagtcNaggattacaggt
629	IGR2281a_1	a/c		Verified	genomic	144	catctgcattatataaagaataac
630	IGR2281a_2	other/w +	Poly t	Verified	genomic	87	aaattaattttttcttccNttttttt
631	IGR2281a_3	a/t		Not yet verified	genomic	72	taattttttaaataaatttttttcttc
632	IGR2283a_2	ins/del	ins/del 2bp t on ref. sequence	Verified	genomic	574	ccggctctctNtagttatt
633	IGR2284a_1	t/c		Verified	genomic	486	gccttcactttccaNataccatcagc
634	IGR2284a_2	t/c		Not yet verified	genomic	536	tgccaagtactattNtaacttctgagaatac
635	IGR2285a_1	a/c		Verified	genomic	171	gaaaaatgaagcNggagaaaaaatgaa
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649	IGR2292a_3	a/t		Verified	genomic	282	atggaattgtatcNtccctctttacaga
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651	IGR2294a_1	t/c	c on ref. sequence	Verified	genomic	390	ccctggaaaaaNgggacactcc
652	IGR2294a_2	t/c		Verified	genomic	440	ttagcaaatggNacaccagga
653	IGR2294a_3	t/g		Verified	genomic	481	tcacagatccNatgtccatgga
654	IGR2295a_1	ins/del		Not yet verified	genomic	438	atttgtgttcNgcaatatgtct
655	IGR2295a_2	a/g		Verified	genomic	535	tgcagctgaggNcctcactggtagaa
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657	IGR2297a_2	t/c	c on ref. sequence	Verified	genomic	198	aaaacactcNtcaggata
658	IGR2297a_3	t/g	g on ref. sequence	Verified	genomic	487	ttctaaagaaaaNaatttcaaccca
659	IGR2297a_4	t/c	c on ref. sequence	Verified	genomic	588	gattttgtcaccacNaggctgccctaaaga
660	IGR2297a_5	a/c	c in ref. sequence	Verified	genomic	446	cctacaagccNgaagagag
661	IGR2298a_1	a/g	g in ref. sequence	Not yet verified	genomic	293	tttaaatgtaaatggNctaaatgtctcca
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663	IGR2300a_2	t/c		Verified	genomic	606	ccaataacaggNictgaaatig
664	IGR2303a_1	t/c	c on ref. sequence	Verified	genomic	189	ttttgtatctacNggcaaaatata

665	IGR2303a_2	g/c	g on ref. sequence	Verified	genomic	495	aatatcattagtNataatgagccc
666	IGR2304a_1	t/c		Verified	genomic	483	cttgatgttNgaatggcat
667	IGR2304a_2	a/g		Verified	genomic	667	ggttgagtgtgacaNtacagggtaaaaa
668	IGR2305a_1	a/t		Verified	genomic	253	tttcgagataggaatNctgcataataatcatttgg
669	IGR2308a_1	t/c	c on ref. sequence	Verified	genomic	339	tttgatcctttgtaagaaacNgctagtggcca
670	IGR2308a_2	a/g		Verified	genomic	561	taggtattgtcaaaattgNacigcattataggaca
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672	IGR2310a_1	ins/del		Not yet verified	genomic	273	aattttgtattttNtagtagagatgggt
673	IGR2311a_1	a/g	g in ref. sequence	Verified	genomic	181	gccacgtctggagtgcnGtggcatgatgtgg
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675	IGR2311a_3	ins/del		Not yet verified	genomic	525	caacctctgcctcctctgggtNgcagtctctgcct
676	IGR2313a_1	other/w +	poly A	Not yet verified	genomic	499	aaaaaaaNcaactaag
677	IGR2313a_2	a/g		Not yet verified	genomic	370	taaccaggNtgtttcaggg
678	IGR2313a_3	a/g		Not yet verified	genomic	335	aaatgggggNtggaggagaca
679	IGR2313a_4	t/c		Not yet verified	genomic	531	cagattaaaaNcagtaaat
680	IGR2313a_5	ins/w+	C insert	Not yet verified	genomic	391	agtttggcNatgatagg
681	IGR2314a_1	ins/w+	varying number of GT repeats	Verified	genomic	560	atgttttcaNgtgtgtgtgt
682	IGR2315a_1	a/g		Not yet verified	genomic	369	cttcattgcNaagagtttgc
683	IGR2315a_2	t/c		Not yet verified	genomic	533	taatttcttaNgccctgtcttt
684	IGR2315a_3	a/g	G in ref	Not yet verified	genomic	211	aacatgccNctgaaca

685	IGR2316a_1	a/g	G in ref	Not yet verified	genomic	499	cccaggcttNtaggatga
686	IGR2316a_2	t/c	G in ref	Not yet verified	genomic	565	aaacccctgNtctgataa
687	IGR2316a_3	a/g		Not yet verified	genomic	469	tgaataaaNccccagtc
688	IGR2321a_1	t/c		Not yet verified	genomic		tttgaaaaaNgtcaaatag
689	IGR3000a_1	a/g	a in ref. sequence	Verified	genomic	224	ttttagaaNtgatacttt
690	IGR3000a_2	a/g		Verified	genomic	558	ttaagaaatagtNttctattactalc
691	IGR3002a_1	g/c	g on ref. sequence	Verified	genomic	146	ctggcagNggtcgcaa
692	IGR3002a_2	a/g		Verified	genomic	511	atatgaacNacatagat
693	IGR3003a_1	a/g		Verified	genomic	494	tgaaccccNtcttactt
694	IGR3004a_2	t/c	c on ref. sequence	Verified	genomic	430	gagtggaactctacNgcccagatttctc
695	IGR3004a_3	ins/del		Verified	genomic	285	atttctctctcttNtttcttcttct
696	IGR3005a_1	t/c	t on ref. sequence	Verified	genomic	494	aggagtagNtagatagaa
697	IGR3005a_2	g/c	c on ref. sequence	Verified	genomic	538	agtagcacNactaccca
698	IGR3005a_3	a/c	c in ref. sequence	Verified	genomic	34	cccatgaaggcaccaaNtcaactgcccagt
699	IGR3006a_1	other	gt repeat	Verified	genomic	234	ccagttctgacgatactcNtgtgtgtgtg
700	IGR3006a_2	t/g		Verified	genomic	227	cagttctgacNatcatcgt
701	IGR3007a_1	t/c		Verified	genomic	458	cgtagccaNtgcgcca
702	IGR3007a_2	other/w		Verified	genomic		
703	IGR3008a_1	+	Poly t	Verified	genomic	176	aaalactgtaccctgtgacNttttt
704	IGR3008a_2	t/c		Verified	genomic	147	cacttattaNttaccata
705	IGR3008a_3	a/c		Verified	genomic	339	tgcatacaaNtctcactt
706	IGR3013a_1	t/c	C in ref. sequence	Verified	genomic		atgcaactcNcacttcacc
707	IGR3016a_1	other	gt repeat	Verified	genomic	342	cacatttatatgcNtgtgtgtg
708	IGR3016a_2	a/g	a in ref. sequence	Verified	genomic	637	ctgctgtgtacagctNtgtgttcatttttgc

708	IGR3018a_1	a/g	g in ref. sequence	Verified	genomic	238	gggcacagacacccNccgigtggggccc
709	IGR3018a_2	t/g		Verified	genomic	191	gggcaccgtgttcNtgatcgtttccttta
710	IGR3019a_1	a/g		Verified	genomic	205	ttgttagaaaattttgcccNattgaggctaata
711	IGR3019a_2	a/g		Verified	genomic	388	cagctttattgaagaNgcaatgttacag
712	IGR3020a_1	g/c	g on ref. sequence	Verified	genomic	172	gtcttcgcccggctNgttttagctggtcc
713	IGR3020a_2	a/c	c in ref. sequence	Verified	genomic	349	cttactagcctagaNaacaaataataag
714	IGR3020a_3	a/g	a in ref. sequence	Verified	genomic	542	tataggaactacNataatgttaggtca
715	IGR3022a_1	a/t	t on ref. sequence	Verified	genomic	267	gctggagagctgtNctcactactagcag
716	IGR3023a_1	g/c	c on ref. sequence	Verified	genomic	79	tcctcttagggcaNagtgcagcaggctccc
717	IGR3023a_2	ins/del	ct repeat	Verified	genomic	264	attctctctctNtctctctgatag
718	IGR3023a_3	t/g	g on ref. sequence	Verified	genomic	368	ggcatgatcatatagcNcactgtaactctg
719	IGR3023a_4	t/c	t on ref. sequence	Verified	genomic	580	gggattacagggtgtgaaNcaccatactggctaa
720	IGR3029a_1	a/g	A in ref sequence	Verified	genomic	201	ctggaggtNcacagacagg
721	IGR3029a_2	a/g	A in ref sequence	Verified	genomic	498	agtccaagNacaaagct
722	IGR3030a_1	t/c	T in ref sequence	Verified	genomic	181	attcatgcNtgcctttt
723	IGR3032a_1	a/g	A in ref sequence	Verified	genomic	158	actagggaNgccaaggc
724	IGR3032a_2	g/c	C in ref sequence	Verified	genomic	281	gtaatoccaNctaticggg
725	IGR3035a_2	a/g	G in ref sequence	Verified	genomic	223	gtcaggggaNtgatgaaaa
726	IGR3036a_1	a/g		Verified	genomic	187	aaatacaNtaaaataa
727	IGR3037a_1	a/c		Verified	genomic	521	gggagaaccNtcaccag
728	IGR3038a_2	t/c		not yet verified	genomic	464	aaatacagaaaNacttttgtgtt

729	IGR3039a_1	a/g	G in ref sequence	Verified	genomic		387	gggccagaggNtggagcgaag
730	IGR3040a_2	t/c		Verified	genomic		517	cccgctcacNaggggagg
731	IGR3040a_3	t/c		Verified	genomic		133	acctgagaaNccaacacacga
732	IGR3041a_1	t/c	T in ref sequence	Verified	genomic		331	tcgtcacNnggaagat
733	IGR3042a_1	a/g		Verified	genomic		435	caccctagaNatgatggaa
734	IGR3043a_1	t/c		Verified	genomic		278	atagcccagtgatggNggctggcactgaact
735	IGR3044a_1	t/c		Verified	genomic		477	caggcatcaatgcagaNttagtggttttcaggg
736	IGR3044a_2	t/c		Verified	genomic		513	ctctggcagactttttcNctgtcacatctctcca
737	IGR3045a_1	t/g		Verified	genomic		137	aagcatggagcagtgtagNcaaggaccitgtgga
738	IGR3046a_1	a/g		Verified	genomic		293	tgggccccagtgctNgccccaggggtccaagcc
739	IGR3047a_1	t/g		Verified	genomic		455	cagactctctccctNgccaggaatgtgctttgt
740	IGR3047a_2	a/g		Verified	genomic		522	ttgactggcctgtgccNggactggggagagtaa
741	IGR3047a_3	t/c		Verified	genomic		609	gtgatgtctctactcNgtcgcattacatagca
742	IGR3049a_1	t/c		Verified	genomic		437	tttatcacacctNattctgcagcagacaga
743	IGR3049a_2	t/c		Verified	genomic		611	gtccacgggcctgcctgNltgccagacggggctcc
744	IGR3050a_1	t/c		Verified	genomic		224	ttctgaatactgagatcNgaagaagtgctctcc
745	IGR3051a_1	a/t		Verified	genomic		667	tttagagatagaaggaaNggaaggctgttagat
746	IGR3053a_1	a/g		Verified	genomic		364	ggggtccttagaaaNggctttcttaggaa
747	IGR3053a_2	t/c		Verified	genomic		481	gttaacagtgacatggNggcccagtgaggagac
748	IGR3054a_1	other/w + t/c	poly A	Verified	genomic		597	ccagtgattggtNaaaaaaaa
749	IGR3055a_1	other/w + t/c	Poly a	Verified	genomic		375	ccctctccaccatNctccagcagaaggacag
750	IGR3055a_2	other/w + a/g		Verified	genomic		133	aaaaaaaaaaaaNttgcttaatcatt
751	IGR3056a_1	a/g		Verified	genomic		328	cttcaaaaaagatgacaNtaatacctgtctctagg
752	IGR3056a_2	a/g		Verified	genomic		383	aaatatcagtgagcNctgacacattacaggcc
753	IGR3057a_1	t/g		Verified	genomic		549	ttagcagtcacictctcattcNctacttctctagcccc
754	IGR3059a_1	a/t		Not yet verified	genomic		94	tatatatatatatNatttcacggtttgggtcta

755	IGR3059a_2	other/w	at repeat	Verified	genomic	63	caacaacNtatatatata
756	IGR3060a_1	g/c		Verified	genomic	102	tccactgttaaggNctctggaattcttt
757	IGR3061a_1	t/c		Verified	genomic	362	tttaattattgataNttttacitccagaagt
758	IGR3061a_2	t/c		Verified	genomic	592	caatattgtcatcNacttttaaaagcatgacttc
759	IGR3062a_2	t/c		Verified	genomic	139	tgaacataattataaNggcgaccttatgccttaa
760	IGR3064a_1	t/c		Verified	genomic	616	ctggcaaggatagtgactttcttgaataaaa
761	IGR3065a_1	a/g		Verified	genomic	358	tttaccatttttaatacaNgltgtctttttattgctgag
762	IGR3066a_1	a/t		Verified	genomic	351	tcTggaagttgcgcctgNaccTgcctccagctcttg
763	IGR3068a_1	t/c		Not yet verified	genomic	337	gaagttcccNgtttagcaggg
764	IGR3072a_1	ins/del	caaa repeat	Verified	genomic	383	caaaacaaacaaacaaacaaaNaactagccggg
765	IGR3072a_2	a/t	t on ref. sequence	Verified	genomic	578	taaaataaaataaaaaNaaaacgaaaaataattt
766	IGR3078a_1	a/g		Verified	genomic	313	gggcaggaggagtgNcaagcactagag
767	IGR3079a_1	a/g		Not yet verified	genomic	120	octcgaataaagtcNctctcagtatac
768	IGR3081a_1	t/g	t on ref. sequence	Verified	genomic	317	gagtcctattcttcttNggggtgcacaccgg
769	IGR3081a_2	a/g		Verified	genomic	286	gaaacgaccagNaatgcgcctcgcg
770	IGR3083a_1	g/c	g on ref. sequence	Not yet verified	genomic	397	gctcgggcgcgtNgccccgggccagacccca
771	IGR3084a_1	t/c	t on ref. sequence	Verified	genomic	504	cggcaggctgNcagagcttt
772	IGR3086a_1	a/t		Verified	genomic	234	ttgagatggtNltggcgatgacc
773	IGR3087a_1	other/w	Poly t	Verified	genomic	325	ggaacaatctcNtttt
774	IGR3087a_2	ins/del		Verified	genomic	90	ttccagattNgacataa
775	IGR3087a_3	t/c		Verified	genomic	185	gtatgtaaaNctctatctg
776	IGR3088a_1	other/w	Poly t	Verified	genomic	108	tgataagctctgcNtttttt
777	IGR3088a_2	a/t	t on ref. sequence	Verified	genomic	269	gcaaacaccNccacacca
778	IGR3089a_1	a/g		Verified	genomic	559	ctagaacaaaaaNgtaagaaaaaa
779	IGR3090a_1	g/c		Verified	genomic	558	agttgctaNaacatctgt



		other/w +	Poly a	Verified	genomic		257		actccgtctcNaaaaaaaaa
780	IGR3095a_1			Not yet verified	genomic		178		aaattgcttNaccggaggc
781	IGR3095a_2	a/t	t on ref. sequence	Verified	genomic		316		cciggagaaNagctgagaa
782	IGR3096a_1	t/c		Verified	genomic		406		aggTggcacNgatctctaaa
783	IGR3096a_2	a/g		Verified	genomic		424		aaagctgtccNgctgcc
784	IGR3096a_3	t/c		Verified	genomic		338		agaaatcatgagagcagNaaaggagagaaaggg ta
785	IGR3097a_1	a/g		Verified	genomic		472		acaacaacaacaaNaaaaagagctcaaatgg
786	IGR3097a_2	a/c		Verified	genomic		373		gctttgtaaaaacNacaaatttattata
787	IGR3098a_1	a/t		Verified	genomic		243		ggcaggcgcatcNagggtcaagagatccaga
788	IGR3100a_1	t/c		Verified	genomic		326		aaggggcNgacatggc
789	IGR3103a_1	t/c		Verified	genomic		231		agtgtgNgatcttgg
790	IGR3105a_1	t/c		Verified	genomic		575		ttaccatNtaaccaa
791	IGR3105a_2	a/g		Verified	genomic		187		tgtgtgNagacagaatcttg
792	IGR3105a_3	ins/w+	CA repeat	Verified	genomic		348		ggttcccNggccagg
793	IGR3108a_1	t/c		Verified	genomic				
794	IGR3110a_1	ins/w+	GAA repeat or deletion	Verified	genomic		59		ggaaagaNgaagaag
795	IGR3111a_1	a/g		Verified	genomic		199		cttgaggNgtgtgct
796	IGR3112a_1	t/c		Verified	genomic		72		ttacttgNccagcttcc
797	IGR3113a_1	g/c	G in ref	Not yet verified	genomic		321		aatggatNtatgtcaga
798	IGR3113a_2	a/t	T in ref	Not yet verified	genomic		368		agggacccNaatagttt
799	IGR3113a_3	t/g	T in ref	Not yet verified	genomic		477		attcagaNgtgtgt
800	IGR3114a_1	a/g		Verified	genomic		571		cacaagttNtccacagag
801	IGR3115a_1	other/w +	poly t	Verified	genomic		557		gaatgatgcNtttttttt
802	IGR3117a_1	t/c		Verified	genomic		452		cccaaagtNtaccttat
803	IGR3118a_1	t/c	C in ref	Not yet verified	genomic		116		tggcataNagaaggtt
804	IGR3119a_1	a/c		Verified	genomic		301		gcctagatcNcttgttgca
805	IGR3119a_2	a/c		Verified	genomic		534		ggccatggtNtatggcc

806	IGR3121a_1	g/c	G in ref	Not yet verified	genomic	586	agtaactggNaccctgggc
807	IGR3122a_1	t/g	G in ref	Not yet verified	genomic	144	catgttcNactacact
808	IGR3122a_2	a/g		Verified	genomic	441	gtaccagcNgctagtggga
809	IGR3125a_1	del/w+	del of ACTGT from ref	Verified	genomic	3121	aaatgggNactgtctcg
810	IGR3125a_2	a/c	C in ref	Not yet verified	genomic	384	ggcaaacNcaccacg
811	IGR3129a_1	t/c		Verified	genomic	193	cctgtggaNttggggt
812	IGR3131a_1	t/g		Verified	genomic	1308	tgtgtgtgNgggtctga
813	IGR3133a_1	a/g		Verified	genomic	2029	tcgggcaNgcatgca
814	IGR3133a_2	t/g		Verified	genomic	2301	ttttagtNtgagtcgc
815	IGR3134a_1	a/g		Verified	genomic	2594	gcctcaNtggatttt
816	IGR3138a_1	a/g		Verified	genomic	508	agctcctNccctcag
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818	IGR3145a_1	a/c		Verified	genomic	373	gaaaggaNtgaaatgc
819	IGR3145a_2	a/g		Verified	genomic	420	gcctgcaNcaactgic
820	IGR3145a_3	ins/w+	polymorphic CAAA	Verified	genomic	379	aaaggactgaaaNgccccagagggc
821	IGR3148a_1	t/c		Verified	genomic	1733	ttcacaccNggaaagct
822	IGR3149a_1	a/g		Verified	genomic	2119	aggaaacNttcttct
823	IGR3150a_1	a/g		Verified	genomic	262	ccagagaNgtaacagaa
824	IGR3152a_1	t/c		Verified	genomic	1223	gccgggcNgatagcct
825	IGR3153a_1	other/w					
826	IGR3153a_2	+	CA repeat	Verified	genomic	1817	ttgcgtaNacacaca
827	IGR3158a_1	g/c		Verified	genomic	2055	gaactggaNagaagcttc
828	IGR3159a_1	a/c		Verified	genomic	669	gggagacNcctttac
829	IGR3159a_2	ins/w+		Verified	genomic	1004	gtgtgtgNgggggg
830	IGR3161a_1	g/c		Verified	genomic	2042	gctgagaNcctatcat
831	IGR3162a_1	a/g		Verified	genomic	2539	gcctctNiatgcag
832	IGR3162a_2	a/g		Verified	genomic	2686	tgggacaNgaacaac
833	IGR3162a_3	a/g		Verified	genomic	2816	cctfcccNtgaggccc
834	IGR3162a_4	g/c		Verified	genomic	2959	cagccccNtcicccc
835	IGR3163a_1	t/c		Verified	genomic	478	gacagtaNagcctgtga
835	IGR3166a_1	a/g		Verified	genomic	325	gcctctatNaggtgcagg

836	IGR3166a_2	other/w +	poly t	Verified	genomic	651	ccatcctcNtttttt
837	IGR3169a_1	a/g		Verified	genomic	40	tgctgccNagtccagt
838	IGR3169a_2	t/c	t in ref	Not yet verified	genomic	505	aacggagtNtgcctct
839	IGR3170a_1	t/g		Verified	genomic	73	gtgtgaNagttaa
840	IGR3170a_2	t/c		Verified	genomic	191	cagtcctcNgagaagt
841	IGR3171a_1	t/c		Verified	genomic	213	ttctattaanGggagaatcc
842	IGR3173a_1	a/g		Verified	genomic	126	taaatcccaNatggattc
843	IGR3174a_1	a/c		Verified	genomic	489	aataaataNtcatlatt
844	IGR3176a_1	other/w +	poly t	Verified	genomic	107	cccccaaccNttttt
845	IGR3178a_1	a/g		Verified	genomic	310	ggatcatNtttaagag
846	IGR3178a_2	del/w+		Verified	genomic	279	ggaattgtNaatactt
847	IGR3179a_1	t/c	C in ref	Not yet verified	genomic	554	tcctggcNtcaagggga
848	IGR3181a_1	a/g	G in ref	Not yet verified	genomic	257	gggaccaNgcagaaa
849	IGR3182a_1	a/c	C in ref	Not yet verified	genomic	614	acaaaacNcaaacia
850	IGR3182a_2	a/t		Verified	genomic	620	aacacaaacNaaaaacagggccaa
851	IGR3183a_1	t/g		Verified	genomic	131	aaacaggNccaatgacta
852	IGR3183a_2	other/w +	poly A	Verified	genomic	248	agggaaagNaaaaaaa
853	IGR3185a_1	a/t		Verified	genomic	211	aaacaatcNctacagt
854	IGR3185a_2	g/c	G in ref	Not yet verified	genomic	558	aaaacatNatacagga
855	IGR3185a_3	a/g	G in ref	Not yet verified	genomic	529	aaaagtNaagtccta
856	IGR3186a_1	other/w +	poly t	Verified	genomic	174	gttgcaaNttttttt
857	IGR3186a_2	g/c		Not yet verified	genomic	58	aaaacatNatacagg
858	IGR3188a_1	a/g		Verified	genomic	152	gcactaNccaaaatat
859	IGR3188a_2	a/g	A in ref	Not yet verified	genomic	508	aacaataNcaaatgtt

860	IGR3189a_1	a/g	G in ref	Not yet verified	genomic	139	acctaggNatttcactcc
861	IGR3189a_2	t/c		Verified	genomic	394	gaaagaaNatafatgtg
862	IGR3189a_3	a/g	A in ref	Not yet verified	genomic	429	gttcaaNatctgac
863	IGR3191a_1	a/g		Verified	genomic	215	ccccgcNacctactt
864	IGR3191a_2	t/c		Verified	genomic	246	cacttagNctttatc
865	IGR3192a_1	t/c		Verified	genomic	328	gggagaNccacacct
866	IGR3193a_1	a/g		Verified	genomic	409	gagacaNgagagga
867	IGR3194a_1	t/c	C in ref	Not yet verified	genomic	296	aaaggatNtgggggtctt
868	IGR3196a_1	t/c		Verified	genomic	137	cacacgctNgcgtatgca
869	IGR3196a_2	other/w +	tg repeat	Verified	genomic	177	gcataataaaNgtgtgtgtg
870	IGR3197a_1	other/w +	poly t	Verified	genomic	308	tggtgtgaNttttttt
871	IGR3199a_1	other/w +	poly a	Verified	genomic	131	tgagtctcNaaaaaaa
872	IGR3200a_1	a/g		Verified	genomic	342	ctccaccNttgttcccc
873	IGR3201a_1	a/t	A in ref	Not yet verified	genomic	234	aggactNatctcta
874	IGR3203a_1	a/g		Verified	genomic	538	ctgcttcNaggagcca
875	IGR3205a_1	t/g		Verified	genomic	1035	taatggaNtaaggat
876	IGR3205a_2	a/g		Not yet verified	genomic	548	cacatggttNcaatgtcac
877	IGR3206a_1	t/c		Verified	genomic	1176	aagatctcNagggtg99g
878	IGR3206a_2	g/c		Verified	genomic	1511	gacaggNatgttctat
879	IGR3206a_3	g/c		Verified	genomic	552	gagacaggNatgttctat
880	IGR3207a_1	t/c		Verified	genomic	205	aaaaaaccttNggctgtct
881	IGR3208a_1	a/t		Not yet verified	genomic	206	ctgccccggNttiaccitggg
882	IGR3210a_1	other/w +	Poly T	Verified	genomic	59	ttttgtgtgtgtggNtttttt
883	IGR3222a_1	a/c		Not yet verified	genomic	594	gccacatNtgtcatca
884	IGR3230a_1	t/g		Verified	genomic	462	agagacacacccitgggNagagatgctgg

885	IGR3230a_2	a/g		Not yet verified	genomic	491		cccacttccaaaccNtgcctgg
886	IGR3236a_1	t/g		Not yet verified	genomic	320		gagaggNtgaagt
887	IGR3238a_1	g/c	G in ref	Not yet verified	genomic	280		gggccagNgcaagtt
888	IGR3242a_1	a/g		Not yet verified	genomic	319		aacctaNggggaggg
889	IGR3244a_1	ins/w+		Not yet verified	genomic	91		tcccgNtgcct
890	IGR3248a_1	t/c		Not yet verified	genomic	395		actgtNccaactt
891	IGR3252a_1	other/w +	poly T	Not yet verified	genomic	183		tctaccNtttttt
892	IGR3252a_2	t/g		Verified	genomic	136		gtgctgNggactgaa
893	IGR3266a_1	a/g		Not yet verified	genomic	156		caggtagNatgtcttg
894	IGR3266a_2	a/g		Verified	genomic	185		ccactgggNccctggctt
895	IGR3268a_1	t/c		Not yet verified	genomic	367		tgttgtaNtctctcc
896	IGR3268a_2	t/c		Not yet verified	genomic	385		aggaactgNctcgacat
897	IGR3274a_1	a/g		Verified	genomic	126		ctctaggaNcatttcag
898	IGR3274a_2	a/g		Verified	genomic	284		tgcagaatNcagtgagc
899	IGR3276a_1	other/w +	poly t	Verified	genomic	340		ctctctctcNtttttttttt
900	IGR3276a_2	ins/w+	ins G	Verified	genomic	221		ttctgctgcNtgaatttgg
901	IGR3278a_1	other/w +	poly t	Verified	genomic	69		ctctttatcNtttttttttt
902	IGR3292a_1	other/w +	poly t	Verified	genomic	518		ttcatctcNtttttttttt
903	IGR3294a_1	t/c	T in ref	Verified	genomic	366		aatftatcctctcttttcaagaaNttgaatttttgaatct
904	IGR3298a_1	a/g		Not yet verified	genomic	76		gtctctccgNtttttccac
905	IGR3300a_2	g/c		Verified	genomic	366		ccfagagggcatcaaaaNtcaaatatgatcaa
906	IGR3302a_1	a/g		Verified	genomic	218		calctcattgtatcNgtccctgattggg

genetic data, which may be used for research purposes only. The data is not to be used for clinical or diagnostic purposes.

907	IGR3304a_1	ins/w+		Verified	genomic	319	tttggagggtgaggtagggNggatcaggagggtca
908	IGR3310a_1	a/g		Not yet verified	genomic	361	ggag
909	IGR3310a_4	other/w +	poly a	Not yet verified	genomic	86	ggaccaaNctgggggtg
910	IGR3312a_1	ins/w+		Verified	genomic	249	aaaaaaaaNgttcccc
911	IGR3324a_1	t/c		Not yet verified	genomic	388	cagataagcatcagatttgNaaacttacaatggga atg
912	IGR3326a_1	other/w +	tg repeat	Verified	genomic	261	tattgtattccaattNtggatgtagccacca
913	IGR3326a_3	t/g		Verified	genomic	295	tattctagtcgtggagaggNttttgtttgtttgtttg
914	IGR3328a_1	t/c		Verified	genomic	586	ttgttttNtttagacagagtctca
915	IGR3330a_1	other/w +	poly t	Verified	genomic	200	tatatatttagttttcatNgtgaattctctttgacc
916	IGR3330a_2	other/w +	poly t	Verified	genomic	512	tacctcNtttttt
917	IGR3332a_1	other/w +	Poly A	Verified	genomic	347	tttttttNaaccttaaa
918	IGR3336a_2	other/w +	poly a	Verified	genomic	467	catctcNaaaaaa
919	IGR3340a_1	a/g		Not yet verified	genomic	524	aaaaaaaNgagagag
920	IGR3348a_1	t/c	T in reference	Verified	genomic	91	agactaNcacagaaa
921	IGR3348a_2	a/g	A in reference	Verified	genomic	202	ccacatNctctcc
922	IGR3348a_3	a/g	A in reference	Verified	genomic	216	gatgggtNagcatt
923	IGR3348a_5	t/c		Verified	genomic	129	tttcatNtgtttt
924	IGR3348a_6	a/g		Verified	genomic	264	aatgatNgccatt
925	IGR3348a_8	a/g	A in ref	Verified	genomic	618	gttcatNtcttg
926	IGR3348a_9	a/g		Not yet verified	genomic	584	gatttttNataagg
927	IGR3350a_1	g/c	G in Reference	Verified	genomic	77	tctaacNtttaag
928	IGR3350a_10	a/g		Not yet verified	genomic	451	catgagNatggaa
929	IGR3350a_11	t/c	C in reference	Verified	genomic	450	ccgtgcttNattgccc

930	IGR3350a_2	t/c	T in Reference	Verified	genomic	88	gaatgttNttccatt
931	IGR3350a_3	g/c	G in reference	Verified	genomic	236	gatttgNtctcig
932	IGR3350a_4	t/c	C in reference	Verified	genomic	247	tgtttgNctgttg
933	IGR3350a_7	t/c	C in reference	Verified	genomic	321	agttgcNtatcag
934	IGR3350a_8	g/c	C in reference	Verified	genomic	349	ggctgaNacaaig
935	IGR3352a_1	a/g	A in reference	Verified	genomic	282	gggatacNgtggig
936	IGR3352a_2	t/c	T in reference	Verified	genomic	314	ttattgNgtctat
937	IGR3352a_3	t/c	T in reference	Verified	genomic	330	attcttNtctctt
938	IGR3352a_4	a/g		Not yet verified	genomic	177	tgggagNgtgtat
939	IGR3352a_5	t/c	T on reference	Not yet verified	genomic	339	tcctttNtctttt
940	IGR3352a_6	a/g	G in ref	Verified	genomic	547	gtgtcaNttttgga
941	IGR3370a_1	other/w +	poly t	Verified	genomic	354	cttttcNttttttt
942	IGR3370a_2	t/c		Verified	genomic	378	agacagNctgtctc
943	IGR3374a_1	a/t		Verified	genomic	193	ggctatNgaaaaa
944	IGR3378a_1	a/t		Verified	genomic	418	gctggaNcataaag
945	IGR3378a_2	a/t		Verified	genomic	563	cttttNaaaaatagg
946	IGR3388a_1	a/t		Not yet verified	genomic	48	aatctttaNagtaatt
947	IGR3388a_2	other/w +		Not yet verified	genomic	441	gttgaatacNtttttttttt
948	IGR3394a_1	t/c		Not yet verified	genomic	493	ccctacaNgtaaat
949	IGR3406a_1	t/c		Not yet verified	genomic	158	aaatataNacatttat
950	IGR3420a_1	a/g		Not yet verified	genomic	322	cgccttcNataaaa
951	IGR3428a_2	a/g	A in ref	Not yet verified	genomic	278	tataaggNtaagg
952	IGR3454a_1	t/c		Not yet verified	genomic	382	tcccattNttaggtt
953	IGR3454a_2	t/c		Not yet verified	genomic	450	aattagaNcccatttt

954	IGR3456a_1	a/g	G in Reference	Not yet verified	genomic	42	tctccNtttgtt
955	IGR3456a_2	a/t	T in Reference	Not yet verified	genomic	81	gtggthNtagitt
956	IGR3456a_3	t/c	T in reference	Not yet verified	genomic	108	ccttcaNgtcctt
957	IGR3456a_4	a/g	G in Reference	Not yet verified	genomic	109	cttcatNtccctt
958	IGR3456a_5	t/g	T in reference	Not yet verified	genomic	178	actcatNgttgg
959	IGR3456a_6	a/g	G in Reference	Not yet verified	genomic	179	ctcatNtttggc
960	IGR3456a_7	other/w +	Poly T	Not yet verified	genomic	204	ctctctcNtttttt
961	IGR3456a_9	a/g		Not yet verified	genomic	398	catgtcNcctgcaaa
962	IGR3460a_1	g/c	C in Reference	Not yet verified	genomic	118	tttgtgNgcagag
963	IGR3462a_1	other/w +	poly t	Not yet verified	genomic	419	ttttttNgctcatca
964	IGR3466a_1	a/g		Not yet verified	genomic	185	gcctcatgNacccctacc
965	IGR3466a_2	g/c		Not yet verified	genomic	503	ctcacaaaNgctccagt
966	IGR3470a_1	a/t		Not yet verified	genomic	199	gctggaggNaggactag
967	IGR3470a_2	t/c		Not yet verified	genomic	438	gtcaaatNattcattt
968	IGR3470a_3	a/t		Not yet verified	genomic	178	tccagctgaNgatgcagg
969	IGR3470a_4	a/t		Not yet verified	genomic	214	agccctgaNtgggcacca
970	IGR3475a_1	a/c		Verified	genomic	483	caccctgctNtataact
971	IGR3475a_2	t/c		Verified	genomic	490	ctatacaNtggttgg
972	IGR3477a_1	t/g		Verified	genomic	468	ccaggtaagNtgc'tgagtg
973	IGR3479a_1	a/g		Verified	genomic	178	tagtgggNagtctgggc



GenBank accession numbers are provided for the sequences used in this study. The accession numbers are listed in the table below.

974	IGR3479a_2	a/t		Not yet verified	genomic	229	ogtaccanNtagtaat
975	IGR3481a_1	a/t		Not yet verified	genomic	139	ctggagggaNctggggact
976	IGR3483a_1	a/g		Verified	genomic	539	gtgatgggNtgccttaag
977	IGR3483a_2	t/g		Verified	genomic	495	atctgglaaNaggtgtgg
978	IGR3483a_3	a/c		Not yet verified	genomic	135	gaaacaggNgcggtggca
979	IGR3485a_1	a/g		Verified	genomic	198	ctctgaaggNtcatcacag
980	IGR3487a_1	a/t		Not yet verified	genomic	184	ctctcaagcNcctgtagta
981	IGR3493a_1	a/c		Not yet verified	genomic	434	ctcttattaNtcccttccca
982	IGR3493a_2	t/c		Verified	genomic	517	gatgaagganlgggtcatgc
983	IGR3493a_3	a/g		Not yet verified	genomic	534	tgctaccaNgtgagcca
984	IGR3493a_4	g/c		Not yet verified	genomic	542	aggtagccaNcaggatgag
985	IGR3495a_1	a/g		Not yet verified	genomic	195	tcacaacaNaagtctcag
986	IGR3499a_1	t/c		Verified	genomic	467	aggggtggacigtNattgttct
987	IGR3501a_1	other/w +	poly T	Not yet verified	genomic	503	ttcatgaaagacNttttttttttg
988	IGR3505a_1	t/c		Verified	genomic	213	tgccctctcNggcccttgggg
989	IGR3515a_1	a/g		Verified	genomic	604	agtgtgggagtgNaacciccagc
990	IGR3515a_2	t/g		Not yet verified	genomic	440	ctccttcgNccagggtga
991	IGR3519a_1	t/c		Verified	genomic	230	tttcctccctNcccctgccica
992	IGR3523a_1	t/c	T in ref	Verified	genomic	193	cacggccagNagccctctg
993	IGR3525a_1	t/g		Verified	genomic	322	ttcagaggggtgNggtgggtcaagt
994	IGR3527a_1	t/c		Verified	genomic	87	cactgtggNctgagctcg
995	IGR3529a_1	a/g		Verified	genomic	251	catgtacaggNgacagatctgg
996	IGR3529a_2	t/c		Verified	genomic	120	aagtgtctNtgaatgtga
997	IGR3531a_1	t/c		Not yet verified	genomic	361	tcaacccctgNattgtacaa
998	IGR3533a_1	a/g		Verified	genomic	137	cacagggagNgtttgaga

999	IGR3535a_1	g/c		Not yet verified	genomic	462		cttgtcttNgtggggagga
###	IGR3535a_2	a/t		Not yet verified	genomic	363		tcgagcctgNctgatggcaaa
###	IGR3537a_1	a/g		Verified	genomic	426		ggagggttagNgcagaagtt
###	IGR3551a_1	a/c		Not yet verified	genomic	403		ggccatccaNcagaaac
###	IGR3553a_2	a/g		Verified	genomic	125		tccccacNctgatcac
###	IGR3553a_3	t/c		Verified	genomic	426		gaattgacctaNggagtagcg
###	IGR3555a_1	t/c		Verified	genomic	188		actgcagcctNgacctcca
###	IGR3563a_1	a/g		Verified	genomic	655		ttccgggtcaNagtaacct
###	IGRX100a_1	a/g		Not yet verified	genomic	142		acccgttNataattc
###	IGRX320a_1	t/c		Not yet verified	genomic	383		tctaaactNgggggaaa
###	IGRX320a_2	other/w +	poly t	Not yet verified	genomic	393		ggggaaacNttttt
###	IGRX460a_1	other/w +	poly t	Not yet verified	genomic	292		ttttttNgagatgga
###	IGRX610a_1	t/c		Not yet verified	genomic	684		attcctgNgttggcct
###	IGRX610a_2	a/g		Not yet verified	genomic	827		tttgctcNgctgcct
###	IGRX650a_1	a/g		Not yet verified	genomic	344		atcagggtNattttta
###	IGRX660a_1	a/g		Not yet verified	genomic	203		tctagtgaNgacacccag
###	IGRX665a_1	other/w +	poly A	Not yet verified	genomic	309		acagatcttNaaaaaa
###	IL13_5240	a/g		Verified	gene	n/a	Interleukin 13	aaacttttcgcgaggggacNgttcaactgaaactc gaaagcatcat
###	IL13_5710	a/g		Verified	gene	n/a	Interleukin 13	ttggggaagagactgtggcgtNgcacttggagcca agggttcaga
###	IL13_5770	a/c		Verified	gene	n/a	Interleukin 13	agcactaaagcagtggaNcccaggagtcctcgtt aataagt
###	IL13_5940	c/t		Verified	gene	n/a	Interleukin 13	cgagtaattatgtttttcttNgtatttaaaataaata tgtt

###	IL3_4400	c/t		Verified	gene	n/a	Interleukin 3	cgaagctccatgaccagacaacgNcctgaag acaagctgggttaactgtctaactga
###	IL4ex1_2495	c/t		Verified	gene	n/a	Interleukin 4	tcgttagctctcctgataaaactaattgNctcacattgt cactgcaaatcgacacct
###	IL4pro_1940	c/t		Verified	gene	n/a	Interleukin 4	acacctaacttgggagaaactgtNccccagtg tgggtaggaga
###	IL5pro3	c/t		Verified	gene	n/a	Interleukin 5	tgctatgaacagaatacataNagatcaggaggt ctggacatcatc
###	IL9_4616	a/g		Verified	gene	n/a	Interleukin 9	tgtgaatggtgatgccaaacctgtttgaacNcaaa aggatgataaagtgggaattggta
###	IL9_4616	a/g		Verified	gene	n/a	Interleukin 9	gtgaatggtgatgccaaacctgtttgaacNcaaaa ggatgataaagtgggaattgg
###	IL9_6085	c/t		Verified	gene	n/a	Interleukin 9	tctctgtaacagccatgcaaccaaaacaaNggca ggcaacgcgtgacat
###	IL9_6085	c/t		Verified	gene	n/a	Interleukin 9	ccctgtaacagccatgcaaccaaaacaaNggcag gcaacgcgtgacat
###	IRF1ex1_1	g/c		Verified	gene	n/a	Interferon regulatory factor 1	aagacgtgcgccgagccccgcgaaNcgagg ccaccggagccgtgccagt
###	IRF1pro1_2	c/t		Verified	gene	n/a	Interferon regulatory factor 1	cacggggcagggtaggcttctgcttNcttcacttc cccagggcagggtgagt
###	IRFex6_1	t/c		Verified	gene	n/a	Interferon regulatory factor 1	ctgacctgtggggtcnccctgccagacct
###	IRFex9_1	t/g		Verified	gene	n/a	Interferon regulatory factor 1	gccactccgactnctcaagagctg
###	IRFex9_2	t/g		Verified	gene	n/a	Interferon regulatory factor 1	tccatccacgttnttggctgccactc
###	IRFpro1_1	a/g		Verified	gene	n/a	Interferon regulatory factor 1	gtagggtatattattttatggtt ggggcagggtaggcttctgcttNcttcactcccc
###	IRFpro1_2	t/c		Verified	gene	n/a	Interferon regulatory factor 1	agggcagggtgagt
###	OCTex5_1	a/g		Verified	gene	n/a	carnitine transporter (organic cation transporter) 1	gaatacaataatcacctgctgtgacagctNtgtgttca tttttcagcttttttga
###	OCTN1ex1_1	g/c		Verified	gene	n/a	carnitine transporter (organic cation transporter) 1	gctgttagaaattggggcgcgaaNccgggggacc gttcctgggaaaca

###	OCTN1ex3_1	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 1	gccctgagtcaggcatcaatgcagaNttagtgtttt tcagggtctggcag
###	OCTN1ex6_1	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 1	ggatatctgcatttcagggtcacttattaNttaccata gcagcaagacataatgg
###	OCTN1ex6_2	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 1	cttatgcatgcaactctcacttcaccttgac
###	OCTN1ex9_1	a/g		Verified	gene		n/a	carnitine transporter (organic cation transporter) 1	ctcagtcattgtgacagatgttcctttgNtagagttc ttgcctaccagattctc
###	OCTN2ex1_1	a/g		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	gtcgcgccccggctccagccccNagcgccgagaa gtggcgatgg
###	OCTN2ex3_1	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	accctgtccccttgaggacatcacagNtgtctcc agaaaggtaggtgatg
###	OCTN2ex3_2	a/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	tctcggctcacagtgcccattgcta
###	OCTN2ex4_1	a/g		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	gccagtggcacatggggcacaNggtcacactc accaccaga
###	OCTN2ex4_2	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	actcaccaccagatgccacgcaNagcaccccc ggcatcgtcagcgcc
###	OCTN2ex6_1	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	aacttccctaggcctgtcagtaaNaaatcagagtg aatgaaaatgagga
###	OCTN2ex6_2	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	tatccttttcactctctgatgacaNaggctttgaatttg tctgaggg
###	OCTN2ex7_1	g/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	gcaagttaggagtaicaagcgaaaNccaaaata gcccactgatagtgct

###	Polyex3_1	t/g		Verified	gene	n/a	Prolyl 4 hydroxylase	gcctataagaggaacccctttgagaggNtgatgtgg ggctggcctgggttactctatg
###	Polyex6_1	t/c		Verified	gene	n/a	Prolyl 4 hydroxylase	ctatccagtggtctcaggcttcttctgaagNgggaat ctcttccctaacca
###	Rad50ex16_1	ins/del other/w	ins/del caa	Verified	gene	n/a	RAD50	ttctctgttaNaaagactgaa
###	Rad50ex16_2	ta repeat		Verified	gene	n/a	RAD50	agactgtctcNaaaaataaaa
###	Rad50ex16_3	ins/del other/w	ins/del t	Verified	gene	n/a	RAD50	ttaaaataatttNacaaaaaacat
###	Rad50ex25a_1	ca repeat		Verified	gene	n/a	RAD50	atttaggaNcccccccc
###	Rad50ex4_1	t/c		Verified	gene	n/a	RAD50	cttctgcttttaaaNttttctgttaaaaag
###	Rad50ex4_2	t/c		Verified	gene	n/a	RAD50	ttaatggactacaaagtNtatttaagggttaca
###	Rad50ex7_1	a/t		Verified	gene	n/a	RAD50	gagattcttattcaNacagaaaaatgataacat
###	Sept2ex10b_1	a/g		Verified	gene	n/a	Septin-like	ttctaaatattttttgNcaccagcggtcaagacaa
###	Sept2ex10c_1	a/g		Verified	gene	n/a	Septin-like	attaagactcccaagcNaatcctgcataattcaa
###	Sept2ex10d_1	t/c		Verified	gene	n/a	Septin-like	gtgtgtgtccacNgaggcacgg
###	Sept2ex10f_1	a/g		Verified	gene	n/a	Septin-like	tccctgttaagtNgggctcatgga
###	Sept2ex2_1	g/c		Not yet verified	gene	n/a	Septin-like	tgtcaggggctgNcctcagaca
###	Sept2ex3_1	t/c		Verified	gene	n/a	Septin-like	cccagacctaNacacctccagga
###	TCF_1625	c/t		Verified	gene	n/a	t cell transcription factor 1	cacttgcctgcagggtgccccgaaaggacNtggg ggataaaattcaaaaaaaagtgtgat

Table 4. Summary of best SNPs in chromosome 5 region.

	SNP marker name	Approxim ate Physical position <sup>1</sup>	SNP type	Tran smitt ed allel e	Frequen cy of allele <sup>2</sup>	Trans mitted	Untra nsmitt ed	C <sup>2</sup>	p-value
5	IGR2055 a 1	435.0	G/T	G	0.357	87	39	18.29	0.000019
	IGR2060 a 1	437.5	C/G	C	0.351	81	34	19.21	0.000012
10	IGR2063 b 1	439.0	C/G	G	0.359	87	37	20.16	0.000007
	IGR2069 a 2	442.0	C/T	T	0.627	52	20	14.22	0.00016
	IGR2078 a 1	446.5	A/G	A	0.364	48	16	16.00	0.000063
15	IGR2096 a 1	455.5	A/C	A	0.349	75	32	17.28	0.000032
	IGR2198 a 1	506.5	C/G	G	0.364	87	41	16.53	0.000048
20	IGR2230 a 1	522.5	C/T	T	0.415	67	28	16.01	0.000063
	IGR2277 a 1	546.0	A/G	G	0.417	79	37	15.21	0.000096
	IGR3081 a 1	609.0	G/T	G	0.338	79	35	16.98	0.000038
25	IGR3096 a 1	616.5	C/T	C	0.429	89	42	16.86	0.00004
	PROLYL ex3 1	686.5	G/T	T	0.383	79	39	13.56	0.00023

<sup>1</sup> Position (kb) on the 850 kb reference sequence.

30 <sup>2</sup> Frequency of allele calculated from the untransmitted parental chromosomes.

TABLE 5

>IGR2001a  
ggcccgaaaggactgtgccccctccccgtcaaacacccccccccgcgtccccaccaag  
ttctggccggggctgtggagcgtgggtcacctggggggcgaaggactccacatcacggtga  
agtggaggtgctgcagccccacaaagcccgagaagcctgccaggggcgccccgggcgaa  
cggcagtgggcgtgggcccgttctgcagcaccattggcgcgggggaggagagtgtgatc  
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From the foregoing, it is apparent that the invention includes a number of general uses that can be expressed concisely as follows. The invention provides for the use of any of the nucleic acid molecules described herein in the diagnosis or monitoring of diseases, particularly IBD, such as in the genotyping of samples from  
5 individuals to be tested. The invention further provides for the use of any of the nucleic acid molecules in the manufacture of a medicament for the treatment or prophylaxis of such diseases. The invention further provides for the use of any of the nucleic acid molecules as a pharmaceutical.

While this invention has been particularly shown and described with references  
10 to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the scope of the invention encompassed by the appended claims.